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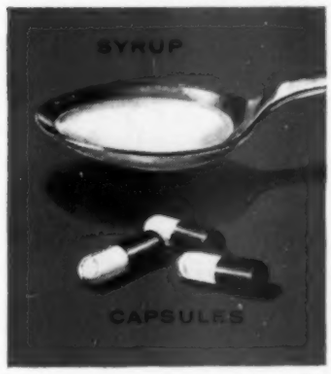

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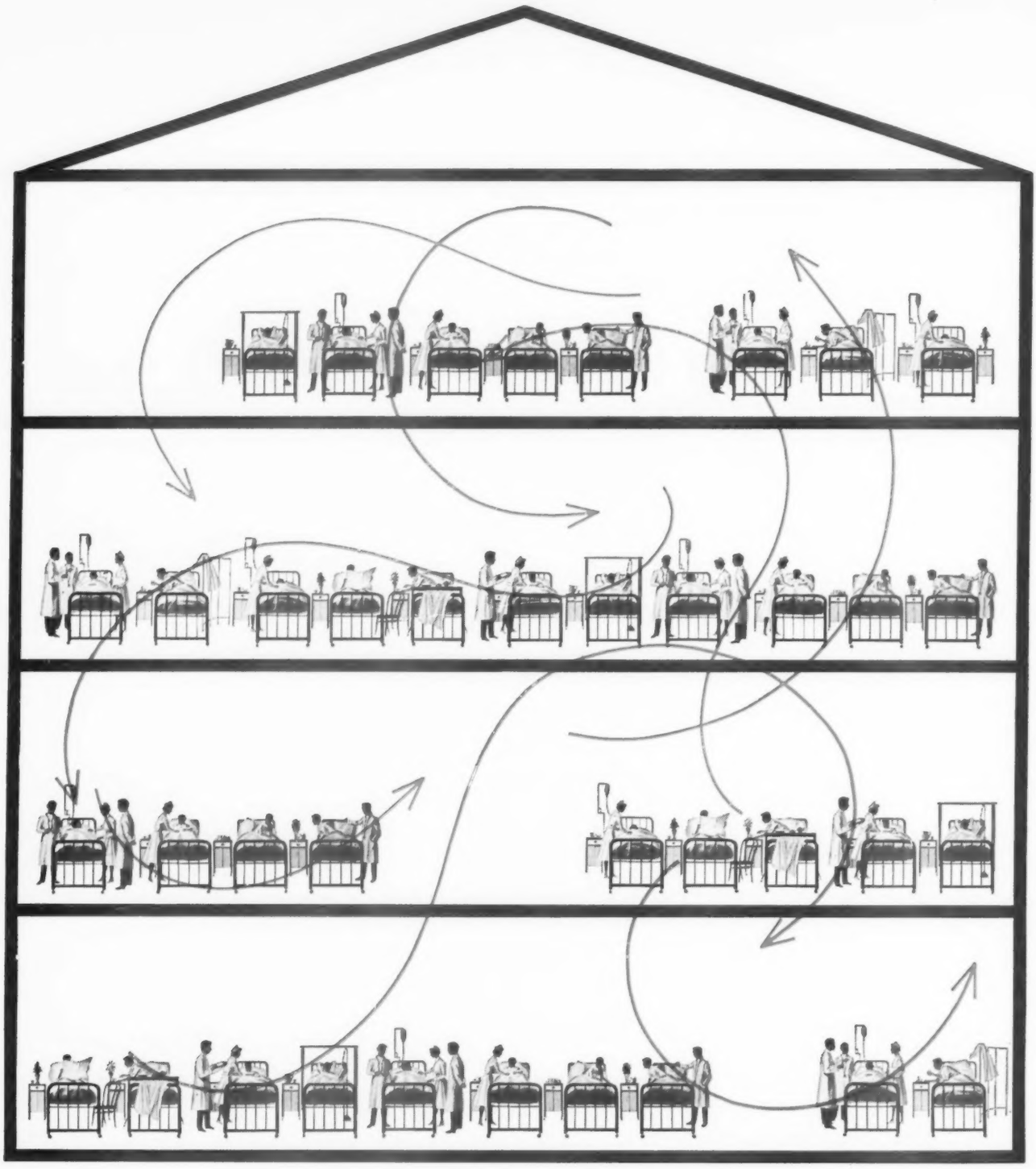

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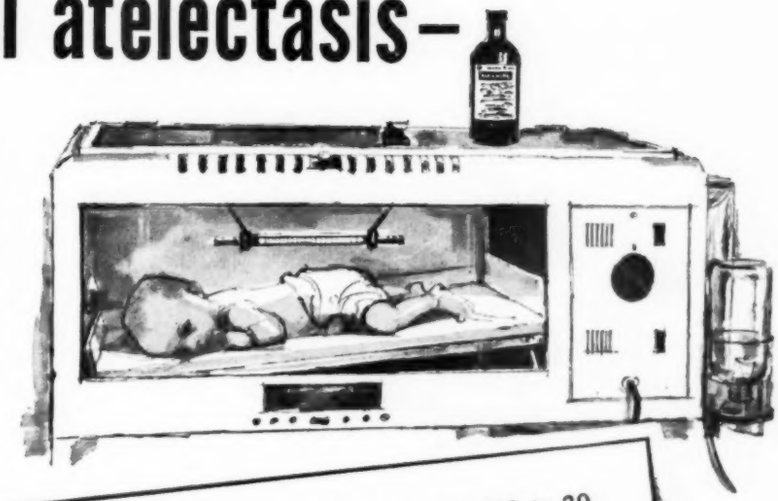

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A typical Alevaire case history—D., a premature male infant (28 to 30 weeks) was delivered as a frank breech. Weight was 3 lb., 6 oz. After birth the patient's condition was poor; shallow, irregular respiration, suprasternal retraction, gasping and cyanosis were present. Breath sounds were diminished, and bilateral atelectatic rales were observed.

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- prevention of postoperative pulmonary complications

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*Smessaert, Andre; Collins, V. J.; and Kracum, V. D.: *New York Jour. Med.*, 55:1587, June 1, 1955.

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News

Latiolais Accepts New Position

Clifton J. Latiolais, formerly Assistant Director of the Audit of Pharmaceutical Service in Hospitals, has recently accepted the position as Director of Pharmacy Service at Ohio State University Health Center, Ohio State University, Columbus. In addition to serving as Director of the Pharmacy Department, Mr. Latiolais holds appointments on the faculties of the Schools of Pharmacy and Medicine.

Mr. Latiolais, currently serving as Vice-President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, has been on the Executive Committee for several years. He is also one of the SOCIETY's representatives to the Joint Committee of the ASHP and the American Hospital Association. He is a graduate of Loyola University College of Pharmacy and holds a Master's Degree from the University of Michigan. Prior to serving as Assistant Director of the Audit of Pharmaceutical Service in Hospitals, he held positions at the University of Chicago Clinics in Chicago and at Strong Memorial Hospital in Rochester, New York.

Booklet on Women in Pharmacy Available

"She Is A Pharmacist," is the title of a career booklet recently published by Kappa Epsilon, a national professional fraternity for women in pharmacy. The booklet has been written by Dr. Eunice Bonow, Assistant Professor of Pharmacy at the University of Wisconsin—Milwaukee. The booklet, written to encourage young women to enter the profession of pharmacy, tells about women pharmacists practicing in the various specialties. "She Is A Pharmacist," relates the experiences of Elizabeth Doty, a high school senior as she visits with Miss Brady, the owner of a community pharmacy; Mrs. Harimon of a prescription pharmacy; Miss Lunde, the chief pharmacist at City Hospital; Miss Randolph of the Pharmacal Laboratories, Inc.; Dr. June Whyte of the pharmacy faculty of the State University; Miss Kerns, a pharmacist-intern and Mrs. Asbury, a relief pharmacist. To complete the account, a sketch of Elizabeth Marshall, who is believed to have been the first woman pharmacist in the United States is included. "She Is A Pharmacist" is available from Dr. Eunice Bonow, 600 W. Kilbourn Ave., Milwaukee 3, Wisconsin. Single copies are twenty-five cents each with a discount on quantity orders.

► *The University of Minnesota College of Pharmacy* has recently received a health research facilities grant in the amount of $76,032 from the United States Public Health Service. The grant is to be used for construction and purchase of equipment for pharmacy research.

► *Geigy Pharmaceuticals,* a Division of Geigy Chemical Corporation, announces the appointment of Dr. Albert Hemming as Director of Promotion.

Dr. Hemming was formerly associated with the Geigy Corporation as Medical Director for some ten years. Prior to his joining Geigy, he served as Assistant Medical Director of Merck & Company, Inc. and as Medical Director for Ciba Pharmaceutical Products.

► *W. L. Arscott,* Vice-President and Director of Sales for E. R. Squibb & Sons, has recently announced the appointment of Paul Freeman to the newly created post of Manager of Professional Relations.

In his new post, Freeman will be responsible for many aspects of Squibb relations with the medical profession. Included among his responsibilities will be special services for medical and professional groups, liaison with medical and pharmaceutical organizations and the supervising of other medico-professional affairs.

Mr. Freeman joined Squibb in 1936 as a salesman and became manager of the Chicago region in 1945. He served in this position until the early part of this year when he acted as regional sales consultant for the Chicago area.

A native of Ironwood, Michigan, Freeman graduated from Ontario College of Pharmacy with a Ph.G. degree and became a registered pharmacist. He practiced his profession in retail pharmacy before joining Squibb.

► *Dr. Clifton F. Lord, Jr.,* has been named head of the Department of Pharmacognosy at the Southern College of Pharmacy in Atlanta. Dr. Lord, who formerly was on the faculty of the University of Buffalo, will also teach courses in hospital pharmacy at the Atlanta school.

► *"Pharmacy, a Noble Profession,"* is the name of a booklet outlining the moral responsibilities of pharmacists in practicing their profession. It is written by the Reverend William L. Wolkovich, Hudson, Mass., a Catholic priest and brother of a pharmacist. The 31 page pamphlet is published by the Daughters of St. Paul, a Roman Catholic order missionary nuns in Boston.

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News

Council Of ASHP Chapters In New York State

There are now 5 organizations which represent the practice of pharmacy in hospitals in the state of New York and are recognized Chapters of the National and parent organization, the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS which is affiliated with the American Pharmaceutical Association. These 5 Affiliated Chapters are: The Southeastern New York State Chapter, Greater New York Chapter, Northeastern New York Society of Hospital Pharmacists, Rochester Area, and the Western New York Chapter. The point to be made here is that there was in the state of New York no single voice representing hospital pharmacy, its practice and practitioners. Therefore, in February, 1958, in Albany, representatives of the 5 Affiliated Chapters decided to form a Council of Hospital Pharmacists in the State of New York. It was proposed that this Council be composed of ten members, which would include either two representatives or their delegates from each Affiliated Chapter. It has been suggested that this Council meet once or twice a year in order to discuss both current problems in hospital pharmacy and to plan for the future development of the practice of hospital pharmacy in the State of New York, as well as for statewide educational efforts such as hospital pharmacy institutes.

On October 8, 1958, the Council met for the second time in New York City with eleven delegates present and all affiliated ASHP Chapters represented. At this meeting, Louis P. Jeffrey of Albany was elected Chairman and Herbert R. Reiman of Buffalo was appointed Secretary.

The meeting was concluded by scheduling the next meeting tentatively to be held in conjunction with the American Pharmaceutical Association Convention in Cincinnati. It is hoped that each chapter will adequately instruct its delegates so that the viewpoint of the whole of New York state hospital pharmacy will be represented by the Council.

Industrial Pharmaceutical Conference

Plans have been completed for the first annual National Industrial Pharmaceutical Conference to be held June 14-17, 1959 at Land O' Lakes, Wisconsin, Louis W. Busse, Associate Dean of the University of Wisconsin School of Pharmacy announced recently.

The conference, the first of its kind in this country, will center around processes concerning compressed tablet manufacture and will give industrial pharmacists an opportunity to discuss industrial problems with fellow workers, Busse said.

Attendance will be limited to 75 pharmaceutical educators and members of pharmaceutical industry, according to Richard S. Strommen, assistant director of Extension Services in Pharmacy, UW Extension Division, who is in charge of arrangements. Strommen said applications for registration will be mailed early in 1959.

"Nationally prominent speakers from both education and industry will present discussion in their fields of specialty," Busse said. "Discussion will include the physics of tablet compression, granulations and their flow properties, the machines used in these processes, and the physical evaluation of the finished tablets."

► *Major General Oliver K. Niess* has been named Surgeon General of the U. S. Air Force. General Niess, who has been Command Surgeon of the Pacific Air Forces in Hawaii, succeeds Major General Dan C. Ogle.

► *"Voluntary Health Insurance in Two Cities,"* is a report of a survey to test the effectiveness of typical voluntary health insurance coverage among insured groups in the population. Published by the Health Information Foundation and written by Dr. Odin W. Anderson, Foundation Research Director, and the staff of the National Opinion Research Center of the University of Chicago, the survey was carried out among those insured by Blue Cross and Blue Shield in Boston, Mass. and Birmingham, Ala.

van Zile Hyde to International Post

Dr. H. van Zile Hyde has been appointed Assistant to the Surgeon General for International Health. Announcement was made by the Surgeon General, Leroy E. Burney.

Dr. Hyde, who has been chief of the Service's Division of International Health for the last five years, will serve as chief advisor to the Surgeon General on international health affairs. His duties will include liaison with the Department of State and other governmental agencies concerned with international health. He will continue to represent the United States on the Executive Board of the World Health Organization, a position to which he has been appointed by President Eisenhower.

His successor as chief of the Service's Division of International Health is Dr. Horace DeLien, who has directed the health program of the International Cooperation Administration in the Philippines for the past seven years.

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1. Nulsen, R. O. et al.: Am. J. Obst. & Gynec. 65:1048, 1953. 2. Nulsen, R. O.: Concurrent administration of TACE and Ergonovine, Ohio State M. J. *(in press).* 3. Bennet, E. T. and McCann, E. C.: J. Maine Med. Assoc. 45:225, 1954. 4. Eichner, E. et al.: Obst. & Gynec. 6:511, 1955.

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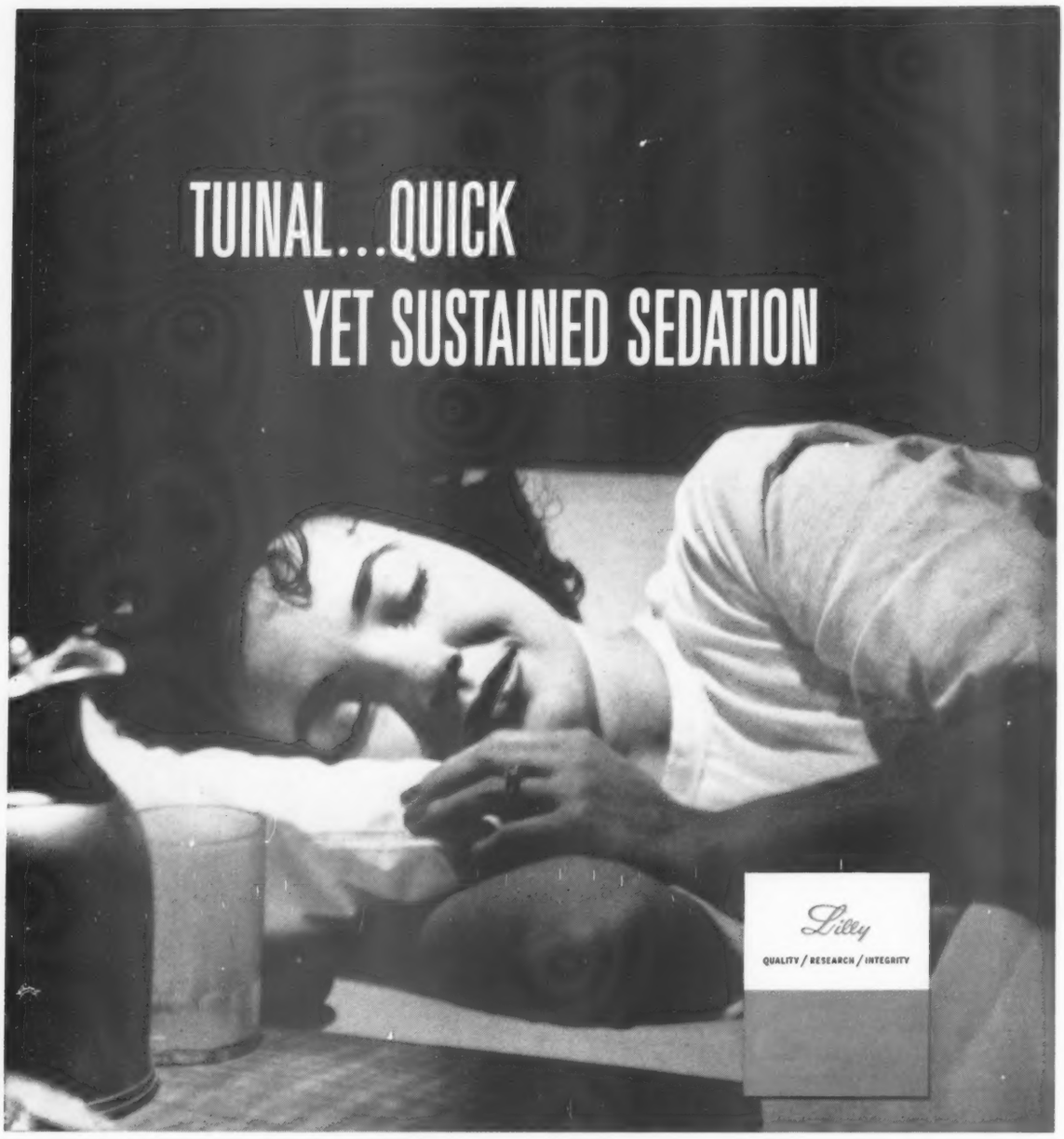

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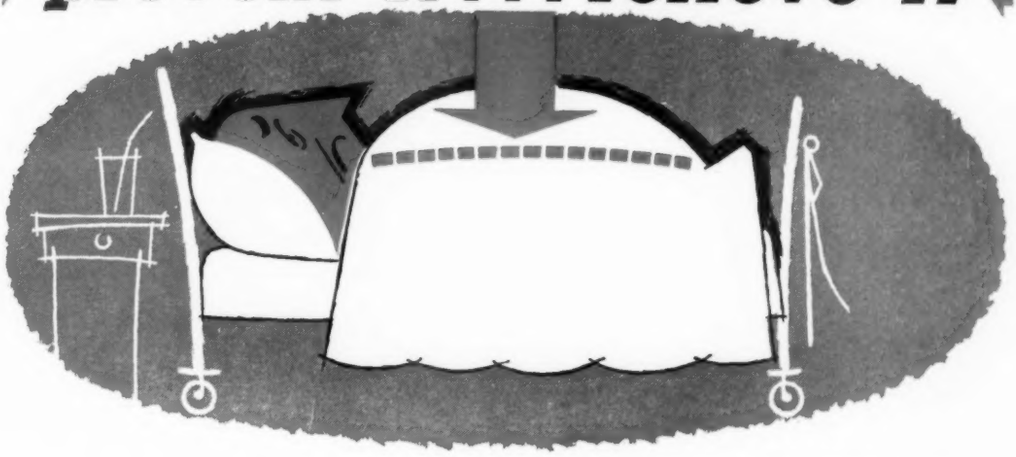

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and as a syrup.

1. Bacala, J.C.: The Use of the Systemic Hemostat, Carbazochrome Salicylate, West J. Surg. *64*:88 (1956).

*U.S. Pat. 2581850; 2506294

Write for comprehensive illustrated brochure describing the action and uses of Adrenosem Salicylate.

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Potassium
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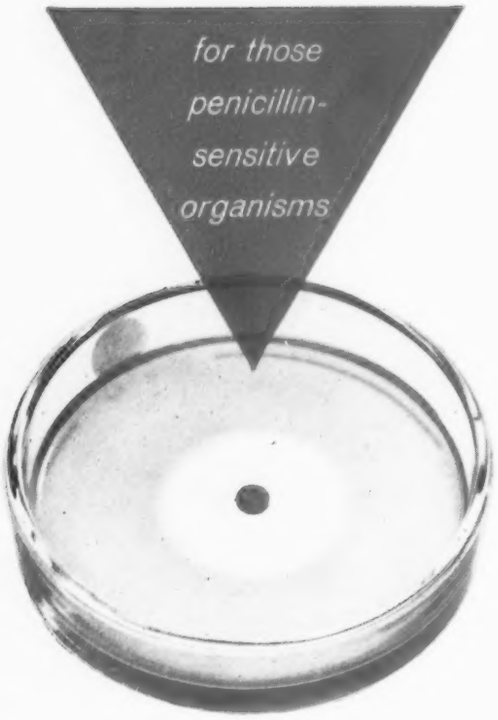

the higher blood levels of

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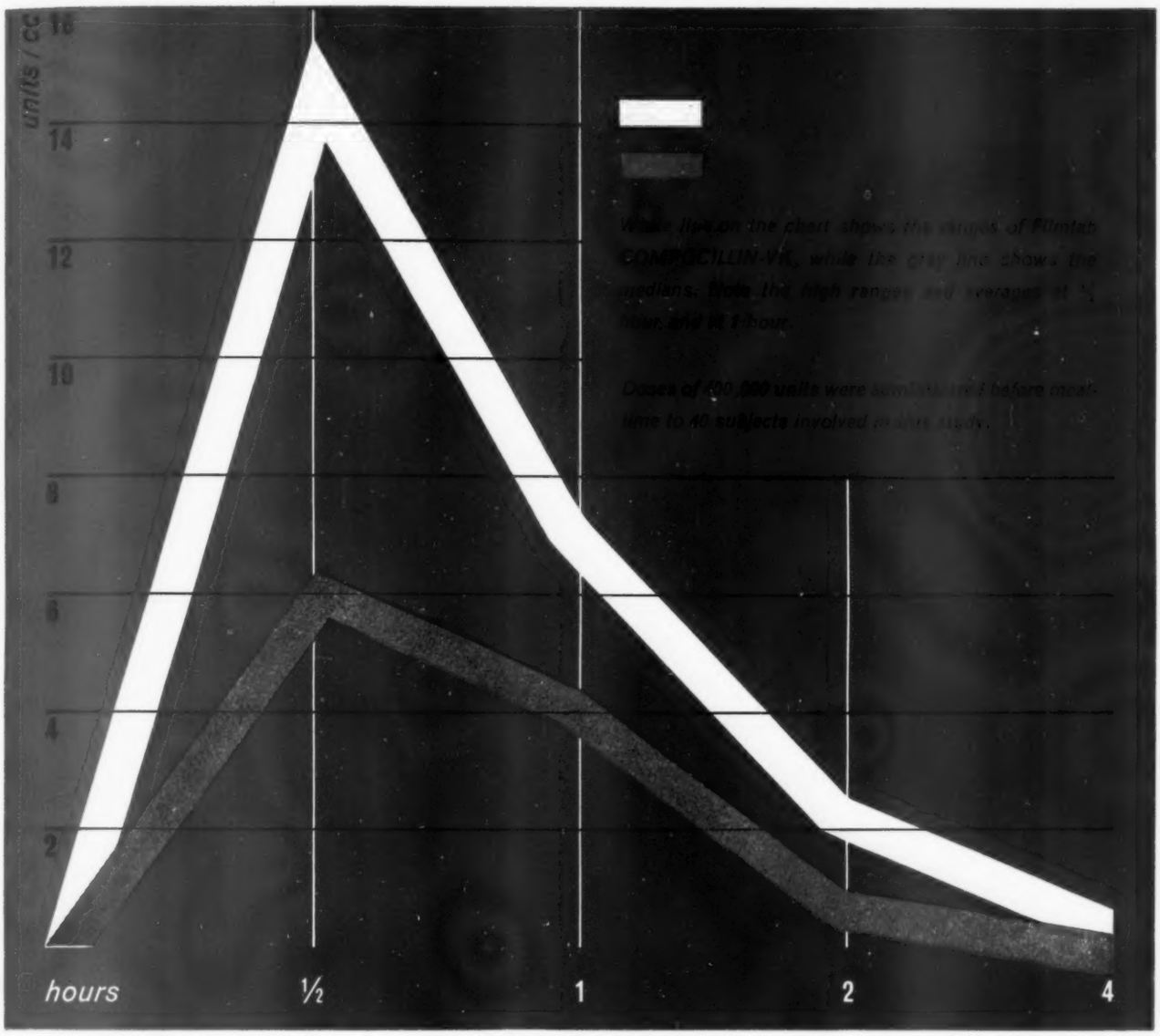

NOW, IN BOTH FILMTAB AND ORAL SOLUTION, patients get high penicillin V blood levels with COMPOCILLIN-VK. Note the chart. Concentrations are three times higher than an equivalent dose of potassium penicillin G.

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Indications:
Against all organisms sensitive to oral penicillin therapy. For prophylaxis and treatment of complications in viral conditions. And as a prophylaxis in rheumatic fever and rheumatic heart disease.

Dosage:
Depending on the severity of the infection, the usual adult dose is 125 to 250 mg. (200,000 to 400,000 units) every four to six hours. For children, dosage may be reduced in proportion to body weight.

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In Filmtabs, representing 125 mg. (200,000 units) of potassium penicillin V, bottles of 50 and 100. In 250 mg. (400,000 units), bottles of 25 and 100.

For Oral Solution, COMPOCILLIN-VK comes in dry granules for easy reconstitution with water. Cherry-flavored, the granules come in 40-cc. and 80-cc. bottles. Each 5-cc. teaspoon of solution represents 125 mg. (200,000 units) of potassium penicillin V.

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Now, after just 12 months, SPONTIN has become an outstanding drug of choice against resistant staphylococci, and in other serious coccal infections.

Six papers presented at the Antibiotics Symposium[1] reported the effectiveness of SPONTIN against resistant staphylococcal infections. Clinical responses involved enterococcal endocarditis, staphylococcal pneumonias and staphylococcal bacteremias. Many of these patients were going downhill steadily—in spite of treatment by other antibiotics.

Toxicity? Careful attention to dosage recommendations has practically eliminated toxicity and side effects as serious obstacles to therapy. Also, recent improvements have been made in the manufacture of SPONTIN; the drug is now made from pure crystals. A recent report[3] in the Journal of the American Medical Association concluded, "It is our opinion that, if proper precautions are observed, ristocetin is a safe and potent agent to employ in the treatment of staphylococcal infections."

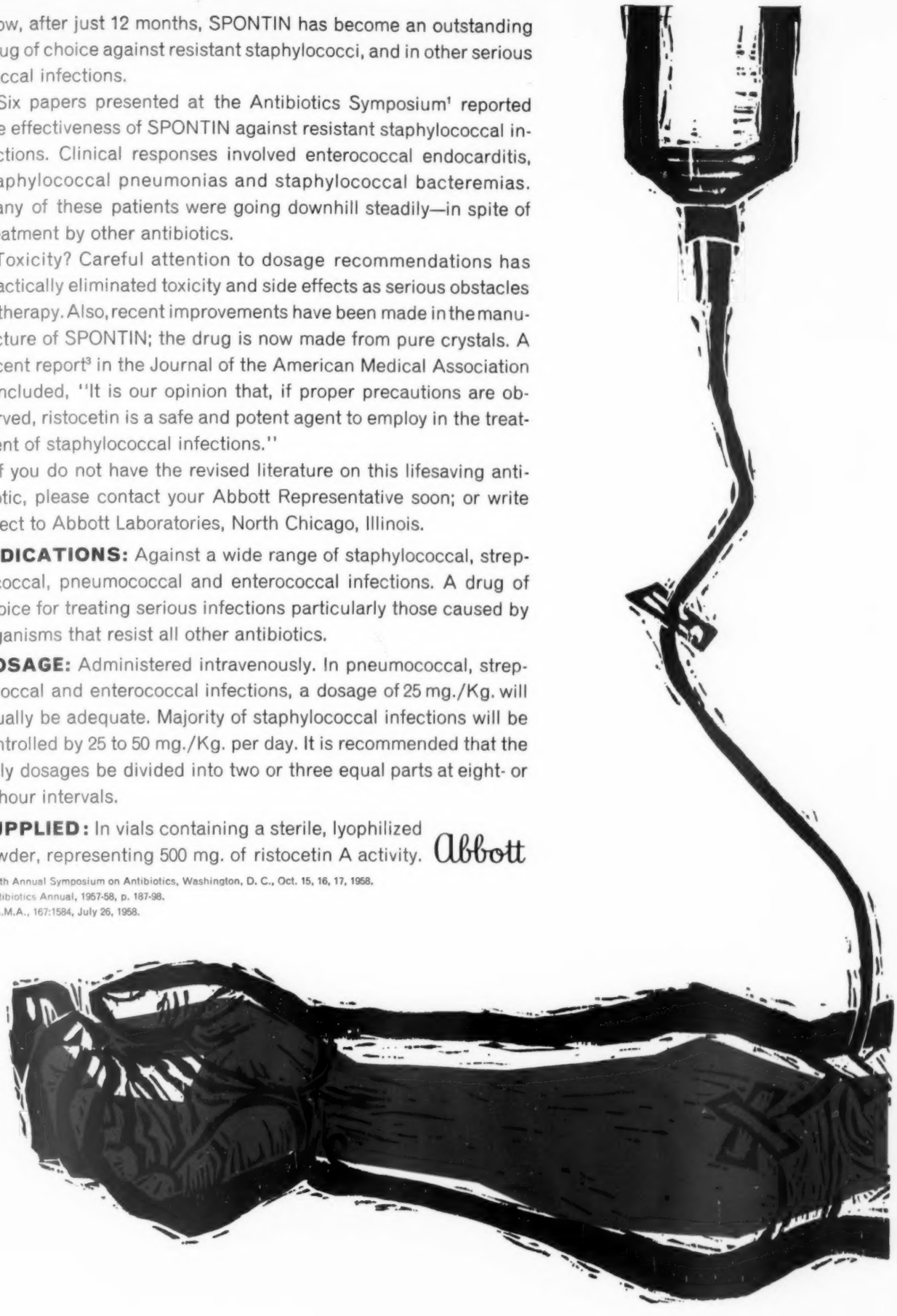
If you do not have the revised literature on this lifesaving antibiotic, please contact your Abbott Representative soon; or write direct to Abbott Laboratories, North Chicago, Illinois.

INDICATIONS: Against a wide range of staphylococcal, streptococcal, pneumococcal and enterococcal infections. A drug of choice for treating serious infections particularly those caused by organisms that resist all other antibiotics.

DOSAGE: Administered intravenously. In pneumococcal, streptococcal and enterococcal infections, a dosage of 25 mg./Kg. will usually be adequate. Majority of staphylococcal infections will be controlled by 25 to 50 mg./Kg. per day. It is recommended that the daily dosages be divided into two or three equal parts at eight- or 12-hour intervals.

SUPPLIED: In vials containing a sterile, lyophilized powder, representing 500 mg. of ristocetin A activity. Abbott

1. Sixth Annual Symposium on Antibiotics, Washington, D. C., Oct. 15, 16, 17, 1958.
2. Antibiotics Annual, 1957-58, p. 187-98.
3. J.A.M.A., 167:1584, July 26, 1958.



Getting the Pill to the Patient

A Candid Look at New Procedures for the Small Hospital Pharmacy

by Alfred A. Mannino
EXECUTIVE DIRECTOR, HOSPITAL DEPT.,
McKESSON & ROBBINS, INC.

Less than half the 7,000 hospitals in the country have accredited pharmacists on their staffs, yet more than 30% of every supply dollar goes for pharmacy purchases. Population is increasing at the rate of more than 7,000 people per day. Disposable incomes continue to spiral. These factors point to a continued expansion in hospitals and hospital services. But while hospitals are growing in number and facilities, the number of trained hospital pharmacists is not keeping pace, and today's shortage will become even more acute as time goes on.

How to provide economical care for the constantly increasing patient load and compensate for the decreasing number of professionally trained personnel, and at the same time cope efficiently with the growing complexities of modern drug buying, is one of the toughest problems facing hospital administrative staffs today.

How are hospitals meeting this challenge? In smaller hospitals, who is responsible for "getting the pill to the patient?" Sometimes it is the general purchasing agent. Often an overworked doctor or nurse —or even the administrator himself. But whoever it is, this extra responsibility is a tremendous burden, especially when you consider the some 7,000 items with which the average hospital pharmacy deals. Obviously, a knowledge of the economic factors of successful management activities, particularly astute buying and inventory procedures, is essential to his success. One serious problem confronting hospitals today is the increasing number of new and nonstandard items. New items, new sizes and duplicates have also become a costly factor. Even storage is a headache. Less than half the country's hospitals are able to handle more than a three-month inventory.

Two keys to efficient hospital pharmacy operation, then, are: standardization and scientific inventory management. But how is the already overburdened person in authority to achieve them without a trained hospital pharmacist?

The answer—and, fortunately, there is an answer—is to look to a supplier of unquestioned integrity and comprehensive services to act as a reliable pharmacy consultant. A good supplier can be counted on to screen and select only drugs and drug products produced by reputable manufacturers, thus insuring reliable merchandise and reduce the need to carry nonstandard items. He will also help maintain a stock level at which the combined costs of *procuring* supplies and *carrying* inventory are at a minimum. And there are countless other services he can offer. Thus, it is important to choose a supplier carefully, to investigate his qualifications and services thoroughly. Here is a checklist of 6 basic questions to aid in his selection:

1. **Will he give you competent professional advice that is honest and unbiased?** (Each one of McKesson's Hospital Service Departments offers the services of a responsible drug therapy consultant—"Rex" McKay®, a trained pharmacy specialist, who is ready to advise on specific problems, to speed emergency delivery service when requested and to keep you abreast of the latest drug developments.)
2. **Does he carry a complete stock of all items you might need?** (McKesson buys from every major drug manufacturer as well as manufacturing under its own label, and researches every new item on the market to determine which manufacturer makes the one best suited to hospital use. McKesson also provides warehouse facilities for bulky items for many small hospitals.)
3. **Does he have the latest information on new developments in the drug field?** (Twice a year, McKesson's Hospital Service Department men undergo intensive training to help them keep up with new products, new methods, new developments that will in turn help hospital pharmacists.)
4. **Does he buy in large quantities direct from manufacturers?** (Whenever quantity purchasing is advantageous, McKesson does so and passes the savings along.)
5. **Does your supplier have national distribution?** (McKesson & Robbins, for example, maintain 82 professionally staffed and completely stocked Hospital Service Departments throughout the country. They service well over half the country's 7,000 hospitals right now and have a total of 125 years' experience in dispensing, manufacturing and distributing drug and pharmaceutical products.)
6. **Is he nearby and readily available?** (McKesson's 82 Hospital Service Units are strategically located throughout the country. They offer a local source of supply that is available any hour of day or night for emergency deliveries as well as routine service.)

Some hospitals, of course, buy direct, but 60% find McKesson & Robbins Hospital Service Departments "just what the doctor ordered." They depend largely on McKesson for economical and efficient management of their hospital pharmacies. McKesson's Hospital Service Departments make a specialty of servicing the small hospital pharmacy and they welcome inquiries on any phase of hospital pharmacy operation. We will send you the name of the McKesson Hospital Service Department nearest you—address inquiry to A. A. Mannino, McKesson & Robbins, 155 East 44 St., New York 17, N. Y.

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a significant advance in cholecystography and cholangiography

diagnosis—greater accuracy, increased gallbladder visualization, high percentage of cholangiograms

ease—no weight calculations, one dosage for all patients

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ORABILEX, Bunamiodyl, is 3(3-butyrylamino-2, 4, 6-triiodophenyl)-2 ethyl sodium acrylate.

ORABILEX Capsules are supplied in envelopes of 6 capsules (0.75 Gm. each). Boxes of 5, 25, and 100 envelopes; also available in hospital size bottles of 250 capsules.

*T.M. ORABILEX is a development of Guerbet Laboratories.

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A Summary Report on

CORTROPHIN®-ZINC

(Corticotropin-Alpha Zinc Hydroxide)

Description

A unique patented electrolytic process (developed by Organon research) produces a complex of *alpha* zinc hydroxide and corticotropin. This complex offers considerable advantages for practical ACTH therapy.

Characteristics

New Cortrophin-Zinc provides corticotropin of unsurpassed purity with low foreign protein content. This reduces the risk of sensitization reactions.

Since about 5% of the corticotropin is uncombined, onset of clinical response is rapid. But the balance, present as a complex of alpha zinc hydroxide, provides a prolonged action so that the effective time span of a single dose is usually several days. Injection of the new electrolytic Cortrophin-Zinc is virtually painless.

Pharmacology

A potent stimulator of cortical activity, Cortrophin-Zinc *does not depress* functioning of the suprarenal glands. Unlike the corticosteroids, adrenocorticotropic hormone arouses the adrenal glands to produce *natural* steroids in natural proportions. In a 5-year study of patients on ACTH therapy, no case of adrenal *or pituitary* depression or atrophy has been observed.

Because Cortrophin-Zinc is virtually painless on injection and its prolonged action obviates frequent injections, it is now practicable to use Cortrophin-Zinc in most of the indications where formerly reliance has been on corticosteroids. This freedom from apprehension of deleterious depressive effects permits clinical use of valuable hormone therapy on a broader scale than has been possible heretofore.

Clinical Uses and Dosage

The many published reports on the use of Cortrophin-Zinc as well as ACTH in thousands of patients indicate its value in over 100 disorders. Most responsive have been: allergies and hypersensitivities, rheumatoid arthritis, bronchial asthma, serum sickness, and inflammatory skin and eye diseases.

Dosage should be individualized, but generally initial control of symptoms is obtained with a single injection of 40 units of Cortrophin-Zinc daily, until control is evident. Maintenance dosage is generally 20 units (or less) twice a week.

Use of Cortrophin-Zinc with oral steroids is now recommended as a safety measure to supply the important suprarenal stimulation and lessen the hazard of atrophy. Periodic use of Cortrophin-Zinc is advocated with all steroid analogs, such as cortisone, hydrocortisone, prednisone, prednisolone, methylprednisone, and triamcinolone.*

Supply

5-cc vials containing 40 and 20 U.S.P. units of corticotropin per cc; 1-cc ampuls containing 40 and 20 U.S.P. units of corticotropin, with sterile disposable syringes.

*Write for complete literature and bibliography containing specific dosage schedules to:

Medical Department

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Western Pennsylvania Society

The first meeting of the fall season of the Western Pennsylvania Society of Hospital Pharmacists was held on September 17 at St. John's Hospital, North Side, Pittsburgh, with Henry West and Harry Strauchler as hosts. This was the seminar business meeting and President Gerard Wolf announced the changes in plans.

Plans are being made to initiate a publication for the Society with the first issue being ready for the Seminar. Regis Kenna has been named Editor with a staff consisting of Charles Rosko, Paul Baumgartner, Gerard Wolf, Rosemarie Slavonic and Ann Marie Peters. In an effort to find an unusual name for the publication, a contest is being sponsored with the winner to be named as the first in a series of articles titled "Pharmacist of the Month."

Election of officers will be held in December of this year and an installation luncheon for the new officers to be sponsored by E. R. Squibb and Sons will be held in January. The nominating committee consists of Paul Baumgartner, *Chairman,* Albert Gerlach and Gerard Wolf.

The Fourth Annual Seminar of the Western Pennsylvania Society of Hospital Pharmacists was held on Wednesday, October 22 at the Mercy Hospital School of Nursing Auditorium. Over one hundred persons from Pennsylvania, Ohio and New York, including hospital pharmacists, administrators, laboratory technicians, medical service representatives and students from the University of Pittsburgh and Duquesne University Schools of Pharmacy, attended the meeting.

Dr. John G. Adams, Dean of the Duquesne University School of Pharmacy, served as moderator of the afternoon session. Greetings were extended by Sister Mary Ferdinand, Mercy Hospital Administrator; Robert M. Sigmond, Director of the Hospital Council of Western Pennsylvania; and E. Burns Geiger of Pfizer Laboratories.

Paul Parker presented the first address of the meeting entitled "The American Hospital Formulary Service and the Use of the Formulary System in Hospitals." Mr. Parker, who had planned to attend as a guest, was pressed into service in the absence of Dr. William Heller who was unable to attend.

Louis Jeffrey, Chief Pharmacist at the Albany Hospital, Albany, N. Y. was the second speaker of the afternoon and he spoke on "A Simple Method of Controlling Drug Samples and Facilitating Communication Between Representatives, Physicians and Pharmacists."

This was followed by the address of the President, Robert C. Bogash. Mr. Bogash gave an interesting presentation on "The Road Ahead for Hospital Pharmacy" in which he dealt with "recognizing the potential of the pharmacy department in the total hospital picture" and citing areas where pharmacy coverage can be extended in the hospital.

A steak dinner was served to the members in the Nursing School Cafeteria. The evening session, consisting of a lively panel discussion on the subject "What's Your Problem?" was the climax of the day. Questions from the audience were presented to panelists including: Jean Sickafoose, Robert Bogash, Burns Geiger, Louis Jeffrey and Paul Parker with President Wolf serving as moderator. Refreshments were served and all agreed that this was the best Seminar held to date. The program was sponsored by Pfizer Laboratories in cooperation with the Western Pennsylvania Society of Hospital Pharmacists.

Participants in the Seminar of the Western Pennsylvania Society. Left to right seated: Robert C. Bogash, Gerard J. Wolf, President of the W.P.S.H.P., Ann Marie Peters, Secretary of the WPSHP, Sister M. Gonzales, R.S.M., Sister M. Francine, O.S.J., Mrs. Jeanne Sickafoose, Sister M. Florentine, Paul Parker. Standing, left to right: Louis P. Jeffrey, Dr. John W. Boenigk, E. Burns Geiger, Dr. John G. Adams, William Sinclair, Treasurer of the WPSHP.

Northeastern New York Chapter

The regular monthly meeting of the Northeastern New York Society of Hospital Pharmacists was held on October 17 at Amsterdam City Hospital in Amsterdam, N. Y. Miss Josephine Stancampiano, Chief Pharmacist, served as hostess and was in charge of arrangements for the evening.

Included on the program was a panel discussion on "Patient Prices in Hospital Pharmacies (Inpatients, Outpatients and Employees)," with the following panel members: Lucy M. Manvel, Leonard Hospital, Troy; Josephine A. Stancampiano, Amsterdam City Hospital, Amsterdam; William H. Hotaling, Ellis Hospital, Schenectady; and Nicholas G. Karalis, Albany Hospital, Albany. There was also a discussion of the "American Hospital Formulary Service," by Louis P. Jeffrey, Chief Pharmacist at Albany Hospital, Albany and President of the Northeastern New York Society.

Members of the Northeastern New York Society also participated in the annual educational trip to E. R. Squibb and Sons in New York City on September 21, 22 and 23.

Washington State Society

The Washington State Society of Hospital Pharmacists sponsored a Seminar in cooperation with Pfizer Laboratories and the University of Washington College of Pharmacy on Saturday, October 11 at the University of Washington, Seattle. Mr. Theodore Taniguchi, Chief Pharmacist at King County Hospital in Seattle, served as seminar moderator. Following a welcome from Dr. Jack Orr, Dean, University of Washington College of Pharmacy; Robert C. Bogash, President, AMERICAN SOCIETY OF HOSPITAL

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PHARMACISTS; Frank Dondero, President, Washington State Society of Hospital Pharmacists; and E. Burns Geiger, Director of Promotions, Pfizer Laboratories, the following papers were presented:

"Potential Sources of Accidents in the Dispensing and Administering of Medications," by Robert C. Bogash, Lenox Hill Hospital, New York City.

"Teaching and Research Responsibilities of the Hospital Pharmacist," by Dr. Nathan A. Hall, Associate Professor of Pharmacy, University of Washington College of Pharmacy.

"Current Studies in Leukemia Therapy," by Dennis M. Donohue, M.D., Clinical Associate in Medicine, University of Washington School of Medicine.

"Public and Professional Relations Program for Hospital Pharmacists," by E. Burns Geiger, Director of Promotions, Pfizer Laboratories.

"Pharmacists As Part of the Hospital Management Team," by Donald A. Faber, Assistant Administrator, Virginia Mason Hospital, Seattle.

The program also included a forum on "Improving Professional Practice" with participants including Robert C. Bogash, Donald A. Faber, John E. Smith, Royal Jubilee Hospital, Victoria, B.C., Canada, Dean Jack E. Orr and E. Burns Geiger. Joseph E. Birmingham, Chief Pharmacist at the Veterans Administration Hospital in Seattle, served as moderator.

The meeting closed with a discussion on "The Road Ahead for Hospital Pharmacy and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS," by Robert C. Bogash.

Southern Appalachian Society

The regular meeting of the Southern Appalachian Society of Hospital Pharmacists was held on Sunday, October 26 at the Charleston General Hospital in Charleston, West Virginia.

The principal speaker was Mr. Robert Simons, Chief Pharmacist of the Memorial Hospital in Wilmington, Delaware. Mr. Simons discussed Poison Controls and the Establishment of Poison Control and Information Centers. He supported his talk with many statistics which emphasized the necessity and importance of the establishment of Poison Control Centers and a Poison Information Service.

Following Mr. Simons' address, reports were heard on surveys conducted by the members on facilities available in their hospitals for emergency treatment of poison cases. As a result of these reports and the subsequent discussion, it was decided that the city of Charleston would be the most ideal location for a Poison Control and Information Center. A committee was appointed to study and present plans for this project.

Southeastern New York Society

The regular meeting of the Southeastern New York State Society of Hospital Pharmacists was held at Mt. Sinai Hospital on Thursday, September 18.

The program for the evening was a discussion of medication errors (or accidents) in hospitals, presented by Mr. Robert Bogash and Mr. Leo Blackman. The presentation was the result of a study undertaken in two large metropolitan hospitals in regard to medication errors, both on the nursing units and in the pharmacy itself. Statistics relating to the type and relative occurrence of accidents involving medication and recommendations for their pre-

Satisfied with the usual cough remedies?

—do you find that the local soothing effect of cough syrups is not enough?

—are you concerned about the side effects of codeine?

—do you find that many remedies decrease cough productivity?

—do you have patients who do not cooperate fully because of cumbersome forms of issue and too frequent dosage?

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SUMMIT, N. J.

vention were given by Mr. Bogash. Mr. Blackman discussed the most frequent types of accidents in the hospital pharmacy and gave illustrations of these incidents. Systems of checks and controls to prevent accidents were also discussed. The meeting was then opened for discussion and members of a panel answered questions relating to medication errors.

The October meeting of the Southeastern New York State Society of Hospital Pharmacists was held at Lenox Hill Hospital on October 16. The program of the evening was an interesting and informative discussion of "Intravenous Fats," by Dr. Parker Vanamee, Chief of Clinical Physiology, Memorial Hospital. Dr. Vanamee related some of the history and problems of obtaining an adequate supply of calories by intravenous infusion and cited some comparisons in the use of amino acids, protein hydrolysates, and dextrose. He then compared these to a new intravenous fat preparation (Lipomul I.V.) and discussed the caloric content and the advantages and disadvantages of its use. Some unusual aspects of its use were discussed, and the program closed with a question and answer period.

A special guest of the evening was Mr. Debebe Biratu, a visitor from Ethiopia who is observing the pharmacy service at the U. S. Public Health Service hospital on Staten Island.

Oregon Society

The Oregon Society of Hospital Pharmacists held a joint meeting with the Oregon Branch of the American Pharmaceutical Association on October 28th at the Imperial Hotel in Portland.

Mr. Robert Resare was installed as President of the Oregon Society, Miss Alma Robertson as Vice-President, and Barbara Christensen as Secretary-Treasurer.

Robert C. Resare (standing) is installed as president of Oregon Society.

Mr. James B. Low, Toastmaster for the evening, introduced the principal speaker, Dr. Joseph B. Trainer, Director of Student Health Service, University of Oregon Medical School.

South Carolina Society

The South Carolina Society of Hospital Pharmacists met in Columbia, S. C., on October 11th. This was a dinner meeting and special guests for the evening were Mr. and Mrs. F. Alex McCracken and Mr. and Mrs. James Plaxco, Sr. Mr. McCracken and Mr. Plaxco are President and Vice-President, respectively, of the South Carolina Pharmaceutical Association.

If not...
here's why you
should try new
Tessalon Perles

- controls cough by dual action—in the chest as well as at cough centers of the brain.
- 2½ times as effective as codeine[1] without the side effects of codeine.
- controls cough frequency without decreasing productivity or expectoration.
- Perles offer convenient, precise dosage and relief for 3 to 8 hours.

AVERAGE ADULT DOSAGE: 100 mg. t.i.d.
In refractory cough, up to 6 perles (600 mg.) a day may be given.

AVERAGE DOSAGE FOR CHILDREN UNDER 10:
One Pediatric Perle (50 mg.) t.i.d.

SUPPLIED: TESSALON *Perles*, 100 mg. (yellow). *Pediatric Perles*, 50 mg. (red).

Pediatric Perles available Oct. 1, 1958.

1. Shane, S. J., Krzyski, T. K., and Copp, S. E.: Canad. M.A.J. 77:600 (Sept. 15) 1957.

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The business of the evening was a report by the Chairman of the Nominating Committee, who made the recommendation that the present officers be asked to continue their duties for another year. This suggestion was accepted and passed unanimously by the members present.

Virginia Society

The work of the Virginia Society of Hospital Pharmacists is transmitted to its membership through a mimeographed sheet known as "The Dispenser." According to the October issue, the group is working on the Minimum Standard for Pharmacies in Hospitals and specific individuals have been appointed to study each section, and report at the November meeting.

Business transacted at the August meeting included a report from the Legislative Committee, approval of a contribution to the A.Ph.A. Building Fund, a suggestion for a scholarship in hospital pharmacy to be sponsored by the Virginia Society of Hospital Pharmacists, and a proposed survey of pharmacy practices in hospitals not having a pharmacist on duty.

Announcement was made of the November 15 meeting which was scheduled in Charlottesville at the University of Virginia Medical School.

Houston Area Society

The Houston Area Society of Hospital Pharmacists held its October meeting at the Mermann Hospital, Houston, on Sunday, October 12. Mr. Robert Lantos, President of the local society, presided. The main business of the meeting was a discussion of the Minimum Standard for Pharmacies in Hospitals. Members had been assigned sections to study and report on, and at the meeting, these reports and suggestions were discussed. Recommendations were compiled and forwarded to the chairman of the Committee on Minimum Standards of the ASHP.

The November meeting of the Houston Area Society was held at the M. D. Anderson Hospital in Houston on November 23. The principal speaker for the evening was Dr. Johanna Blumel of the Department of Orthopedics Research and the University of Texas Medical Branch at Galveston. Dr. Blumel, who is a pharmacist as well as a geneticist, attended the International Pharmaceutical Federation meeting in Brussels in September and presented an account of the meeting and of her visit to Belgium and the surrounding countries.

Mr. Robert Lantos gave a report on the meeting of the ASHP Executive Committee in Indianapolis, and Miss Adela Schneider presented a brief history of the Society in observance of the fifth anniversary of the establishment of the Houston Area chapter.

Michigan Society

The McGregor Memorial Conference Center on the campus of Wayne State University was the site of the November meeting of the Michigan Society of Hospital Pharmacists. The occasion of the meeting was a seminar sponsored jointly by the Wayne State College of Pharmacy, the Michigan Society of Hospital Pharmacists and Pfizer Laboratories.

Greater Kansas City Society

The first Fall meeting of the Greater Kansas City Society of Hospital Pharmacists was held at the Blue Cross-Blue Shield Building on September 9. Business of the meeting included a discussion of the recommendations of the Committee on Safety Practices and Procedures of the ASHP. Consideration was also given to forms used to report drug accidents. The members also heard a proposal to make application to the Medical Society to permit hospital pharmacists to attend medical meetings in the Kansas City area.

Georgia Society

The Georgia Society of Hospital Pharmacists, with the cooperation of the University of Georgia School of Pharmacy and the Center for Continuing Education, held the first Seminar for Hospital Pharmacists in the State of Georgia, in Athens on October 25 and 26. All presidents of state societies affiliated with the Southeastern Society of Hospital Pharmacists were invited to attend.

After an enjoyable day that included a barbecue lunch, a homecoming football game, and an evening banquet, the Society held a business meeting at which the members expressed the need for a liaison committee to work with the State Board of Pharmacy and retail pharmacists to effect a closer relationship between the two groups and the hospital pharmacists. Discussion was held on special projects relating to Minimum Standards and Safety Practices and Procedures, and the meeting was brought to a close after the election of officers to serve for the coming year.

Sunday was devoted to the Seminar portion of the two-day program, with panel discussions on "The Need for Pharmacists in Small Hospitals," "Hospital Forms and Formularies," and "Poison Control Centers." Climaxing the day's program was a talk by Dr. Arthur Purdum, Chief Pharmacist at The Johns Hopkins Hospital, Baltimore, whose subject was "The Future of Hospital Pharmacy."

Adding to the program was the Non-Denominational Church Service held Sunday morning in the Conference Room at the Center for Continuing Education, by the Chaplain of the University of Georgia, Dr. Robert H. Ayers.

The interest in this Seminar was manifest by the attendance and also by a vote of the members participating to make it an annual program to be held at the Center in October of each year.

Dr. W. Arthur Purdum speaks at meeting of Georgia Society. Shown in photo are Jack Kirkland, President of the Southeastern Society; Clara Greene, President of the Georgia Society, Rheta E. Leverett, Secretary of Georgia Society and Dr. Purdum.

Now everybody's talking...

about... *closer control of cross infection in every part of the hospital*

Wider recognition of the current problem of hospital-acquired infections is focusing new attention on ways and means of reducing this hazard to good patient care. Hospital and medical society meetings—and hospital, medical and surgical journals—are daily shedding new light on the varied aspects of the overall problem.

In many hospitals, a special "committee on cross infection" has been appointed to review practices and procedures. In others, each department head is studying closely his or her own methods of operation. Few hospitals exist which are not giving some special thought to this highly current problem.

Out of this critical evaluation has grown an awareness that environmental asepsis is a major weapon for cutting cross infection to a minimum. Application of continuous disinfection procedures from operating rooms through food service and laundry areas can be the means to changing the hospital's entire experience with hospital-acquired respiratory, intestinal, urinary or post-operative wound infections.

Take floors, for instance

Floors offer a great opportunity for furthering the spread of infection. Microorganisms settling to the floor are redispersed on dust particles or tracked through the hospital on shoes. Walls and ceilings as well can be reservoirs of potential infection. Lehn & Fink disinfectants not only kill all the most common pathogens on contact but are continuously active against new contaminants touching the disinfected surface for as long as a week later.

While the patient is there

Concurrent disinfection is practical whether or not the patient is "isolated." Wiping of furniture and fixtures and damp mopping of floor, with a disinfectant, stop air- and floor-borne microbes at the source.

In the operating room

Lehn & Fink disinfectants have many applications here. Among them: mopping floors; cleaning grills, ducts, and coils of air conditioners; as standard equipment on the scrub-up cart; as a germicidal dip to remove gross contamination from gloves before their removal; to gather instruments into enroute to sterilizer.

Other L & F disinfectant applications are many: for disinfection of instruments with lens systems, to wipe and store thermometers, to sanitize utensils, etc. In all instances, action is bactericidal, fungicidal and tuberculocidal.

Which L & F disinfectant?

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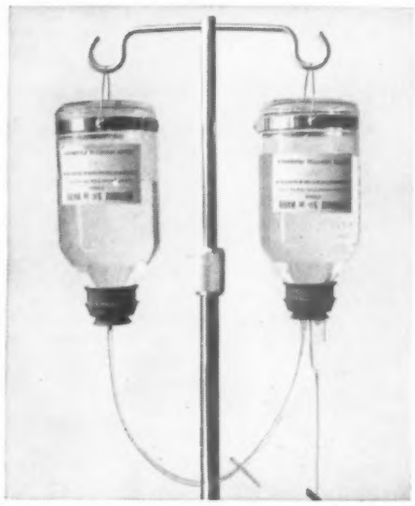

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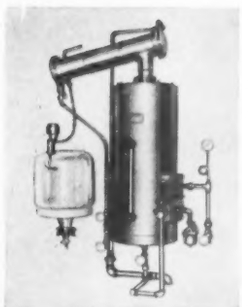

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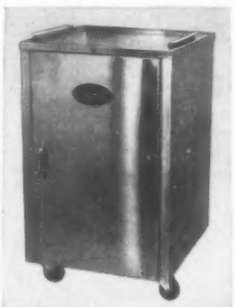

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Lethargy, fatigue and emotional depression secondary to chronic illness in elderly patients; mild depression secondary to short-term illness. (Twenty-three "normal," healthy people also received the drug.)	"For the entire 112 patients 66 per cent showed marked improvements [obvious drug effect and mood improvement] . . ."	"No serious side reactions were noted . . . In no case was it necessary to stop the drug. No evidence of significant effect upon blood pressure or pulse has been found. This is particularly interesting, since these side effects have been common with other mood elevating drugs . . ."[2]
Drug-induced psychophysiologic depression; physiologic after-effects of certain anesthetics; barbiturate intoxication; moribund states due to systemic infection. (All patients were epileptic, mentally retarded and/or brain damaged.)	"All except two [of 129] patients responded to the initial injection [of parenteral Ritalin] within 1½ to 15 minutes."	"In no instance was there any evidence of untoward effects." ". . . the very poor basic physical condition of our patients in this study, those associated with profound chronic brain damage, accentuates the safety of parenteral Ritalin . . ."[3]

DOSAGE: *Oral:* Dosage will depend upon indication and individual response. Many patients respond to 10 mg. b.i.d. or t.i.d. Others will require 20-mg. doses. In a few cases, 5-mg. doses will be adequate. If inability to sleep is encountered, last dose should be given before 6 p.m. *Parenteral:* 10 to 30 mg., intravenously or intramuscularly. RITALIN® hydrochloride (methylphenidate hydrochloride CIBA)

REFERENCES: 1. Natenshon, A. I.: Dis. Nerv. System *17*:392 (Dec.) 1956. 2. Landman, M. E., Preisig, R., and Perlman, M.: J. M. Soc. New Jersey *55*:55 (Feb.) 1958. 3. Carter, C. H., and Maley, M. C.: Dis. Nerv. System *18*:146 (April) 1957.

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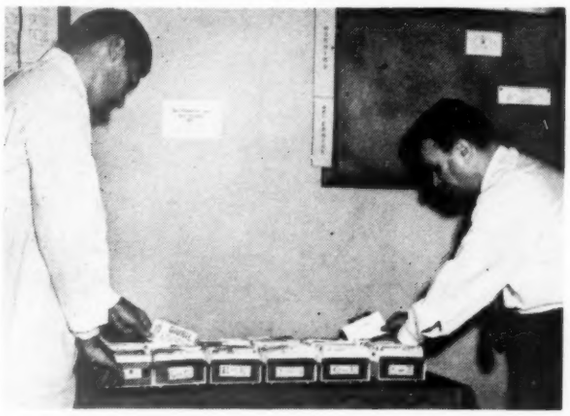
Dear Sirs:

Drug Information Cards

DEAR SIRS: The accompanying photograph showing physicians using our drug information cards may be of interest to your readers. The file as shown here is placed in an office next to the Medical Conference Room and the sign on the wall reads "Drug Information Cards—Help Yourself." The physicians are informed that they may keep the cards for personal use. The files are serviced by pharmacy personnel periodically with old cards being replenished and new ones added.

BENJAMIN TEPLITSKY, *Chief, Pharmacy Service*
Veterans Administration Hospital
Albany, New York



Mr. Benjamin Teplitsky (right) refers to drug information cards which are made available for physicians and staff.

Correction

DEAR SIRS: Would you please insert the following corrections in the next issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY:

Re: Skin Testing Materials for the Diagnosis of Disease, *Am. J. Hosp. Pharm. 15*:122 (Feb.) 1958:

Mumps Skin Test Antigen and Ducrey Antigen are no longer manufactured by Lederle Laboratories.

Pasteurella Tularensis Antigen (Lederle No. 2726) is prepared and distributed for use only in conducting macro agglutination tests. It is not intended for human injection. Any implication that it can be used as such is contrary to safe medical practice as the hazards that may be involved by the administration of this material cannot be predicted.

EDWARD F. CROUMEY
Chief Pharmacist

Mary Fletcher Hospital
Burlington, Vt.

EDITOR'S NOTE: Also in reference to the above article, echinococcus antigen is not available from the National Institutes of Health or from Eli Lilly Company. However, serological tests will be performed on serum by Dr. Irving G. Kagan of the Communicable Disease Center, Chamblee, Georgia.

Formulary Service

DEAR SIRS: On reading the AMERICAN JOURNAL OF HOSPITAL PHARMACY Vol. 15, No. 6 (June 1958), I noted the most interesting article on ASHP Formulary Service. Since we are in the process of establishing a formulary in our hospital, I was most interested. I would appreciate it if you would kindly send and bill me for one copy of your Hospital Formulary of Selected Drugs, when available.

This is a wonderful idea and I for one will avail myself of this new service and arrange to get one for each department in the hospital later on . . .

SISTER M. CLARISSA, *Pharmacist*

St. Bernardine's Hospital
San Bernardino, California

Reprints Requested

DEAR SIRS: Will you please send me at least three reprints of the article entitled "The Role of An Antibiotics Committee of the Medical Staff," which appeared in the June issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Thank you . . .

W. H. HOTALING, *Chief Pharmacist*

Ellis Hospital
Schenectady, N. Y.

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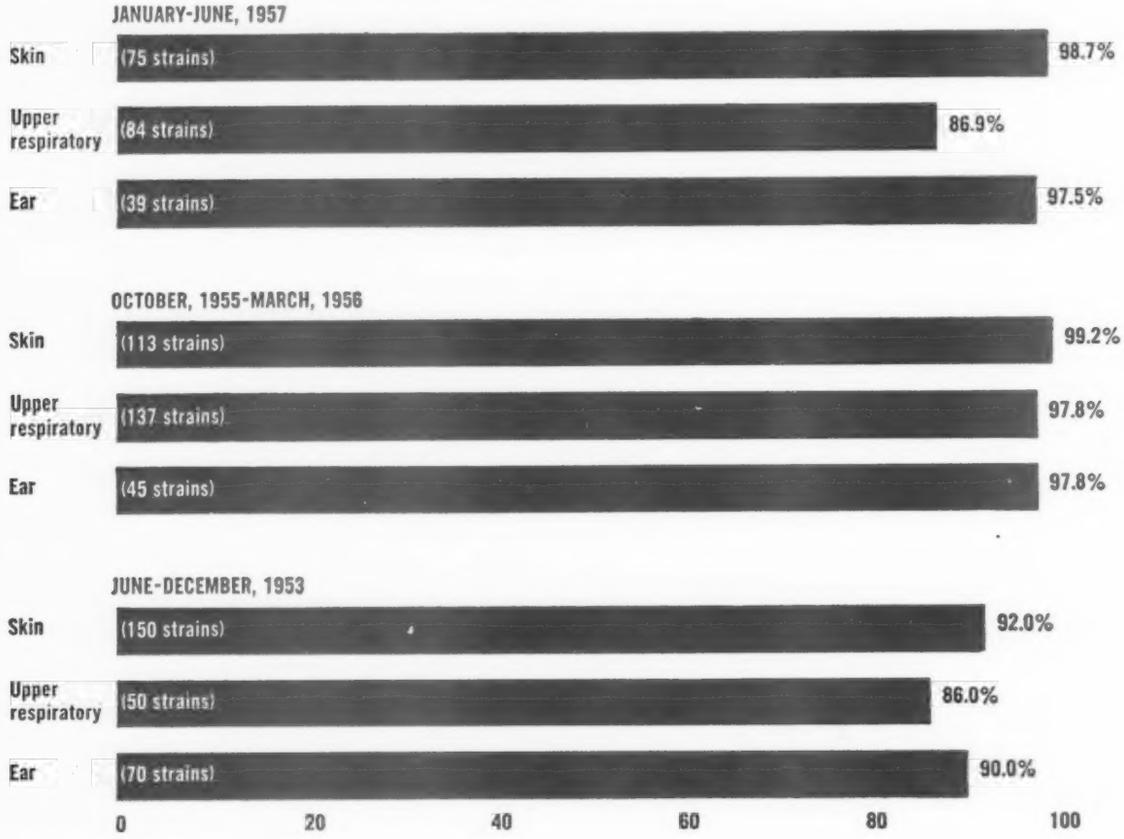

*Adapted from Royer, A., in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 783.

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by DON E. FRANCKE

Use of the Formulary Service

► THE AMERICAN HOSPITAL FORMULARY SERVICE IS NOW being printed and is expected to be ready for distribution in January 1959. Evidence of the need by hospitals for this Service is the almost 2,000 prepublication orders which have been received for it. Orders range from a single copy to several hundred copies. Many who have ordered single copies have indicated their wish to examine the Formulary Service and to have it reviewed by their medical staff before ordering sufficient copies for all nursing units and clinics of the hospital.

Significant of the attitude of hospitals toward the Formulary Service is the approval in principle which has been given to it by the American Hospital Association and the Catholic Hospital Association. The Service has also received similar approval of the American Pharmaceutical Association.

The approaching distribution of the ASHP Formulary Service provides a timely setting for the medical staff of each hospital, working through its Pharmacy and Therapeutics Committee, to re-examine its policies and procedures of operation and to determine what modification, if any, need be made.

Basic in this consideration is a realization that the American Hospital Formulary Service is not a national hospital formulary to be used in the form in which it is distributed. Rather, the intent of the SOCIETY is to supply a comprehensive collection of drug monographs from which the medical staff of each hospital is expected to *select* those drugs which it considers to be the ones of choice. Thus, one of the most important single factors in the ASHP Formulary Service is that the medical staff of each hospital retains complete authority as to the drugs included in the formulary of its hospital.

In re-examining its operational policies and procedures, one of the basic questions to be answered is: Has the medical staff approved the formulary system and has it also approved and adopted clearly written policies and procedures governing its operation? If these basic steps have not been taken, the pharmacist should review for the medical staff, and particularly the Pharmacy and Therapeutics Committee, the fundamental operating principles of the formulary system. Numerous reprints of articles on the formulary system may be obtained from the Division of Hospital Pharmacy at 2215 Constitution Avenue, N. W., Washington, D. C. In his review the pharmacist may wish to refer to the editorial "Ten Guides for the Operation of a Formulary System" (*Bull. Am. Soc. Hosp. Pharm. 14*:663, Nov.-Dec. 1957). After enumerating ten principles of operation, the editorial concludes with the following statement:

"The well-operated formulary system must be guided by principles which are just and fair to the patient, the medical staff, the pharmacy staff, and the hospital. Especially important is the spirit with which the system is operated. If the pharmacist, on whom falls the responsibility of implementing the formulary system, maintains an attitude of helpful cooperation with the medical staff, if he fosters the formulary system as an educational tool for practitioners and students of medicine, nursing and pharmacy, if he encourages the acceptance and use of really new and better drugs as they are developed and evaluated, and if he employs the formulary system to actively promote better patient care—if he does these things and is guided by sound professional principles, the formulary system in his hospital will be well accepted by all."

In his discussion of the use of the Formulary Service the pharmacist will also want to point out that some monographs will still have to be prepared locally, particularly for those preparations which are used primarily in a single hospital or in a group of hospitals. In addition, some provision must be made by the medical staff for making information on investigational drugs available since these will not be in the Formulary Service.

Few hospitals will use all the drug monographs which will be a part of the Formulary Service as it is distributed early next year. In addition, supplementary drug monographs will be issued from time to time during 1959 and in succeeding years. Since the formulary is a dynamic, ever-changing compilation of drugs selected by the medical staff, drugs selected today may be replaced tomorrow and those not selected today may be the drugs of choice tomorrow. Thus, it is necessary for the pharmacist to maintain a file of all currently unused monographs and to distribute to the nursing units only those monographs of drugs which have been selected by the medical staff.

With the appearance of the American Hospital Formulary Service, hospitals and their medical and pharmacy staffs are no longer faced with the tedious, time-consuming task of preparing drug monographs. Rather, there is greater opportunity for the medical staff and its Pharmacy and Therapeutics Committee to devote more time to careful evaluation and selection of drugs and to other matters related to the use of pharmaceuticals in hospitals.

PARTICIPATING IN TOTAL HOSPITAL ACTIVITIES

an opportunity for the pharmacist

by PAUL G. BJERKE

► READING THE REGISTER I FIND THAT SOME of you are from the western part of the United States. I spent a delightful vacation again this year, camping in many of your states. As we passed through the northern part of Arizona the radio announcer was telling how they had finally located the brother of an Arizona man who was seriously ill in New York City. The situation had become particularly acute because the brother was failing very fast. They located the man's brother out bicycling and put both him and the bicycle on the train. Arriving at the hospital, he took one look at his brother, punctured the front bicycle tire, and almost immediately the brother sat up. He punctured the other tire and the man, apparently cured, jumped out of bed and embraced his brother. That, said the announcer, is what Arizona air can do for you!

Are we so concerned with the Pharmacy Department that we either ignore or take very little part in the total activities of the hospital? You and I know our department is the most important in the hospital, but to many it is just a part of the hospital team. A team has its strong members, and it is my purpose to discuss with you how the pharmacist can be an active member of the administrative team.

I have been in hospital pharmacy what to me has been a relatively short time, but measured in years, it dates back to the time when it was a relatively new field. I was the first full-time pharmacist in an institution that now has grown to nearly 300 beds. It was necessary for me to start on a part-time basis until I could prove the necessity of my presence full-time. The School of Pharmacy at the University of Wisconsin was anxious to begin training pharmacists for hospitals, but it was very difficult to get anyone to accept a hospital internship. I can remember very well one of my professors telling me that if I had to return evenings to the pharmacy to put up a shelf or paint the room, by all means put forth the extra effort. I am sure some of you have had similar experiences. Today hospital pharmacy has made such strides that this extra effort can be put forth into something more worthwhile to you, to your department, and to your hospital.

Austin Smith, in addressing the First Annual Philadelphia Pharmacy Forum, said, "We are all beginning to learn more about where we have been so we may know better where we are to go and how to get there."

As an active member of the hospital team, attitude, loyalty and interest are essential. I know this is the type of hospital pharmacist I am talking to today or you wouldn't be here in hope of new ideas.

The Voice of Your Department

Of real importance to the pharmacy is a Pharmacy and Therapeutic Committee. Again, I am sure most of you have such a Committee and have seen its real value. For those of you who are not familiar with the Committee or who are just starting one, I would like to point out that it is appointed by the chief of staff from the various segments of the medical staff. The pharmacist generally serves as its secretary. This Committee can serve as the voice of your department to the medical staff. It can serve as a guide for the drugs used in the hospital. It can advise you and help you make difficult decisions. It can help you in formulating policies, especially those pertaining to the medical staff. It will bring you closer to the staff. This is an essential and very desirous committee in any hospital. This theme will be developed later in the program.

Being close to the medical staff is very desirous; your ability to act as a consultant to the medical staff can make you essential. By making your department a friendly place, the physician is encouraged to drop by. No matter how trivial his problem might seem to you, it may be of great importance to him. Encourage these visits because they can form great bonds. The personal relationship established between the physician and the pharmacist can only be an added pleasure.

It has been the custom of our medical staff occasionally to invite the pharmacist to present a paper to the medical staff. Recognizing that this takes considerable preparation, it is a real opportunity for the pharmacist. Nothing can further your cause more

PAUL G. BJERKE is Chief Pharmacist at Luther Hospital, Eau Claire, Wisconsin.

Presented to the Institute on Hospital Pharmacy, University of Chicago, Illinois, July 28, 1958.

than to be accepted as a consultant to the medical staff on all matters pertaining to drugs. The staff is looking for the unbiased information the hospital pharmacist is able to present. Surely in your role as consultant you will be invited to attend regularly the medical staff meetings and clinico-pathological conferences. The pharmacist is then available should there be a question in his field and, if for no other reason, he will be with the physician where in a relaxed atmosphere mutual problems can be discussed.

Research Activities

Another important phase in helping the physician with his problems is that of carrying on a research program. In my case it is rather limited. Obviously, your staff and equipment will determine your own progress, but research can include many things. Definitely you want to have any problems that concern pharmacy. Don't let the word "research" scare you. Research does not mean that you must undertake to solve a problem as important as the discovery of a new drug. Realize that the development or discovery of anything that is new and useful may be termed research. Each pharmacist is entirely capable of undertaking some phase. The contributions to pharmaceutical science by hospital pharmacists have been of a high order of excellence. The pharmaceutical literature is constantly reporting advancements by our groups. The collections and publications of hospital formularies and books or booklets on hospital pharmacy are included in the term "literary research." This extra routine activity will earn respect and advancement for you and your department.

Glenn Jenkins, Dean of the School of Pharmacy at Purdue University, had this to say about research in the June, 1958 issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY: "Although every hospital pharmacist might engage in some project under the name of research and should be encouraged to do so, the performance of the professional service function stands as an almost insurmountable barrier to research in most hospitals. It has been reported that there are between 150 and 200 large hospitals where research is established as a major activity. Certainly, there must be many more where research is given some support. Each of these large hospitals should provide the possibility of an opportunity for at least one full-time research pharmacist, especially where the hospital is situated in a university environment. Other hospitals provide some opportunity for the service pharmacist who has the interest and ability to do research. It has been said that a man need not be given free time for research; he would find time to do research if he had the spark to do it. There is some truth in this view but the spirit of research does not thrive where time and routine are of first importance.

"Research is the life-blood of science. Science is the source of power for a nation, an industry or a profession in our time. A program to develop research in hospital pharmacy can yield rich dividends in prestige and values for the profession." He also said, "The practitioner level of our profession has given little support to research or to education for research. Hospital pharmacy, which is the highest professional segment of practice, has been the only exception. Even in hospitals research has been relegated to a subordinate position for many reasons, among them: (1) the late emergence from inactivity which changed with the founding of the ASHP, (2) concern with organization, education, accreditation, and other problems, and (3) the lack of trained manpower and facilities. Nevertheless, this SOCIETY has as one of its objectives to promote research in hospital pharmacy practice and in pharmaceutical problems in general. It is natural for research to be in a subordinate position because the three basic functions common to a health profession are: first, the service function which is the reason why the profession is given a special status with certain monopolistic privileges; second, the teaching function which relates to the instruction and upgrading of those entering as well as those practicing the professions and others with whom the professional practitioners work; third, the research function which has for its purpose the discovery of truth and the extension of the service and educational functions."

In England, for example, research is an important function of the pharmacist's work.

Herbert Grainger, Chief Pharmacist at Westminster Hospital in London, England, said in 1952 at a meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in Philadelphia, "The importance of maintaining a small analytical laboratory cannot be overemphasized. First, it is necessary to carry out control analysis on drugs supplied. We do not attempt to analyze all incoming goods as a matter of routine, but there are occasions when it must be done. For example, we prepare our own tincture of opium, etc. from raw opium. An assay of the morphine content is necessary at the time of purchasing the opium, and, of course, on the finished material. Again, with other vegetable drugs such as belladonna leaf or colchicum corm.

"From time to time it is important to check the distilled water from stills. Sometimes there is doubt as to the quality of goods received on contract; for example, the chlorine content of concentrated hypochlorite materials. One could go on at length to cite similar instances. The existence of such a laboratory opens other possibilities of service to the hospital. For example, the arbitration of quality in domestic goods—cleaning materials such as soaps, scouring powders, and etc., purchased by other departments. It is often possible for the pharmacist to effect economies in the

hospital by offering alternatives to some of the commercial preparations available or to devise entirely new ones.

"A flow of work of this kind through the department throws up sufficient problems to keep even the most intrepid and energetic hospital pharmacist with more research items on his list than he can hope to cover."

Teaching Program

The relationship with the medical staff can be strengthened with a teaching program for the intern and resident staff. Such a program will not only benefit the house staff but it will be of great help to the pharmacy. Since the house staff works directly with the medical staff, the things they take from the conferences will be reflected to its medical staff. We have in the past conducted our meetings on Friday from one until two o'clock, meeting each week. When we started we met monthly, but on the insistence of the house staff the meetings were held twice monthly, then weekly. Conferences started with lectures on prescription writing followed with discussion by the pharmacist on various types of products such as antibiotics, sedatives, hormone products, eye preparation, ear preparations, and so forth.

Mr. F. E. Kunkel, a retail pharmacist, in the January, 1957 *Pennsylvania Pharmacist* said: "There is much to say about the need for pharmacists taking the initiative and selling their profession and their services to those who need them most. Six years of experience at our hospital and the meetings with administration throughout the nation have convinced me of the merit of this project, but it is a long slow process to get the idea across to the administrators. The idea of a pharmacist voluntarily offering to be helpful without some hidden axe to grind is unique to many of them and a little hard to accept.

"Developing a cooperative arrangement with a small hospital has effects on physicians and the laity far beyond anything we can achieve in any other manner. One of the most stimulating results of this association has been the sharpening of interest in the professional side of pharmacy. Practicing pharmacy in a truly professional atmosphere and meeting the physician on a basis impossible in a retail pharmacy only adds to pleasure."

Helping the Nursing Staff

We, as hospital pharmacists, have not only responsibilities to the medical staff in our hospitals, but to the nursing staffs as well. I am sure that in your hospital the nursing staff depends on you as a drug consultant. Our literature file can be as valuable to the student and graduate nurse as it is to the physician. The nursing staff should feel free to consult the pharmacist.

Eliminating duplications helps the staff nurse avoid errors and is good economics for proper operation of the department. Whether or not a formulary is maintained or other methods are used to obtain this end, we all know it is desirable in this day of complexity and increased inventories. The nurse, too, has a problem in keeping abreast of present day advances.

Participation in Disaster Plans

I have been dealing with things that are most essential to the operation of your department and your relationship to the medical and nursing staffs. To be most effective we must project ourselves into other phases of the hospital program.

Not long ago we had a disaster in our area. An area nearby was hit by a tornado. We had set up a disaster plan in our hospital, a plan in which the Pharmacy Department was to play an important part. Thanks to wonderful cooperation from everyone it was a smooth operation. I know that in every hospital the pharmacy should have a part in this committee and plan.

Jerome Miller, writing on the role of pharmacists in disaster in the January, 1958 issue of the *American Professional Pharmacist,* said: "Another aspect of the pharmacist's ability which will be in great demand is that of his skill as an organizer. At any disaster there is a large group present which has a tendency to become panicky. The initial shock is great enough so that these people who have this tendency to become panicky will become useful aids in the emergency under skillful leadership. It is when there is time for thought that we find these individuals succumbing to their inherent panic. The pharmacist, utilizing his ability to organize a group into a working and functioning unit, will help lessen the number of individuals who succumb to panic."

Abbott Laboratories has recently released a new film on disaster planning that is available for showing in your hospital. It is intended to be helpful to you in setting up your disaster plan if you do not already have such a plan in effect. I have a copy of our disaster plan with me if anyone is interested in seeing it.

Interdepartmental Activities

As a part of the administrative team the pharmacist will participate in department head meetings. Here is an opportunity for the department head to cooperate with the other members of the team.

The administrator places a high valuation on the ability of the pharmacist to coordinate the activities of his department and other hospital units. Smooth functioning interdepartmental relationships are evi-

dence that department heads accept responsibility as part of the hospital's management team. Interdepartmental difficulties are the bane of administration because they lead inevitably to decreased efficiency in the hospital objective of providing a high quality of patient care at a reasonable cost.

Since the head of the Pharmacy Department is a part of the management, there are a number of specific areas in which the administrator expects help and cooperative and thoughtful effort from him. First, obviously, it is paramount that the patient be given a high quality of pharmaceutical service at a reasonable cost. Administrators as well as pharmacists recognize that a total pharmacy service means much more than the mere compounding and dispensing of drugs.

Of the many hospital committees, you can be of great help on the Health Committee or as an advisor to it. An important consideration of an inoculation program can be its advisability or its cost. Many times administration, unfamiliar with these problems, will need your advice. Because you are widely read, your opinion on the necessity of various programs will be advisable. I am sure one of the problems that will be so discussed will be that of further immunization against Asian flu this fall. You are in an important position to advise and assist in any health program that your hospital might be considering. Of course, you will be limited by the time you have or the extra time you want to give to these efforts.

Community Relations Programs

There are many facets of activity in which you can assist the hospital. This may be in helping the public relations program of your hospital.

It was my responsibility to publish a booklet commemorating the opening of a new addition to our hospital. The theme of the fourteen-page bulletin was "Luther Hospital Builds." Through a series of pictures and short descriptions, we tried to show the public what they bought and what they had gained. The booklet, through the same type of pictures and short descriptions, then took the reader on a tour through the entire hospital, starting at the registration desk and going through each department, showing how each contributed to the welfare of the patient. It included a tribute to those employees with over 25 years of service and concluded with a picture of the medical staff and directors. While this publication included the entire hospital, it is an example of what a hospital pharmacist can do in the way of public relations.

In any public relations program, whether it be your pharmacy or that of your institution, good press and radio relations are very important.

National Hospital Day, May 12, was also my responsibility in our hospital. After developing a theme around the completion of our building program and our hospital as an educational center, the press was invited to visit us. The reporter gave us an excellent story and, moreover, the radio gave us top billing on its news broadcast. This was essential to the success of that day. Another phase of the program was the conducting of tours by the student nurses. A definite tour was planned and each guide was given a plan of the route with a few facts concerning each department. The student nurses were taken on the tour previous to the opening. As they approached the Pharmacy, for example, they told the approximate number of prescriptions filled last year and that, like many other departments, the Pharmacy must operate on a twenty-four hour basis. If there were any questions, the pharmacist was there to answer them. It is things such as these that impress the public with the kind of pharmaceutical service a hospital is able to give its patients.

Inasmuch as the Pharmacy is concerned, I think the people of your community should know that you are here in Chicago attending this Institute, that you have been appointed on this board or that council, that you have been recognized for this service or that accomplishment, or that you have attended a state or national meeting. That is good public relations for your department, your hospital, and you. That relationship with the public should not be neglected. If it is not neglected the patient will feel and know that the preparation of his drugs when he is a patient in your hospital will be in capable hands. I am as cognizant as anyone that public relations can be overdone, but perhaps this is not as bad as no public relations at all.

S. H. Dretzka, Secretary of the Wisconsin State Board of Pharmacy, has said: "The wise hospital administrator will consider the Pharmacy as one of the institution's greatest assets in its public relations program. He will arrange for the Pharmacy to be located in a prominent spot where the public will see it and appreciate its professional prestige and efficiency.

"Many of a hospital's most interesting services must necessarily be carried on behind closed doors. The sterile equipment of surgery cannot be opened to public view. Fascinating vital research and testing in orderly, attractive laboratories cannot be carried on in public. But, the efficient, professional business of pharmaceutical services can be shown and may arouse tremendous interest and admiration. The hospital pharmacy can and should be a most effective public relations medium."

Someone said some months ago, "It is surprising how many educated people regard science as an affair of laboratories, apparatus and formulas rather than as an attitude of the mind." This is important in any walk of life but especially so for you and me. The professional man must do more than offer the service normally expected from those in his profession. A

professional man is judged for what he does and not for what he represents.

As a highly respected member of the management team you should expect to participate in activities that may not, at your first thought, seem to fall into the realm of your activities; however, they do and it is so important for you to participate.

Other Avenues

An active pharmacist has so many avenues of participation in any hospital. Perhaps there is need for someone to head up the drive for Community Chest, or United Fund for your hospital. Perhaps the Red Cross is having difficulty in your community finding blood donors. Why not have your leadership spearhead the drive for donors in your hospital?

As the drug specialist and as a representative of your hospital, you may be called upon to speak to various groups. These may include the hospital guild, nurses' institutes or meetings, dental societies, health departments, hospital associations, and civic club or groups in the community. All are important in building prestige.

Next month our hospital plans to open a Diagnostic and Outpatient Center. Besides tours for the public, service clubs will be invited to visit the center and hold their regular weekly meetings there. As a part of the team, the pharmacist can play an interesting and important role in activities such as these.

As a service to the patient, the hospital, the staff and the community, the establishment of a Poison Information Service can be a very helpful service.

Our SOCIETY'S Economic and Household Poison Committee, along with the Academy of Pediatrics and general practice groups, has had considerable influence in stimulating more interest in this important area. Many states have established information centers and each hospital pharmacist should take the lead in his hospital to establish a reliable and fast service for the treatment of poison cases.

I can hear some of you taking a deep breath and wondering how you are expected to do this besides running your own department. Obviously, your department is your first consideration, but the many things I have suggested are ways of improving your participation in the total activities of the hospital. Remember, too, that all these things are not going to be done in a week, month, or even a year.

Leadership Qualities

Fred Macarow, in *Management Revue,* has said, "With the expansion of scientific and technical progress, management must move faster in order to prepare for the job ahead. Every organized effort requires order, managerial technique and leadership. Everyone can benefit from a systematic program of developing the qualities of leadership essential to good management and to effective direction and coordination of the efforts of subordinates.

"There is a distinction between leadership and teamwork. Teamwork cannot exist without leadership, but leadership can exist without team play.

"Leadership must be coupled with teamwork if the purposes of an organization are to be secured. Frequently, the leader must subordinate his own personal desire to the interest of the team.

"The leader must give his subordinates maximum leeway possible in determining their own method of approach because that in itself develops their leadership ability; however, the leader must be sure that when he has decided that it is necessary to use a particular method of approach, he can depend on his subordinates to pull as a team without hesitation.

"The qualities of leadership and team play meet their sternest test when a decision is indicated for divergent points of view. In such cases the leader must have a thorough understanding of what effects the decision will have at the lower levels as well as the broad implications that the decision has at higher levels of management.

"The job of an executive requires constant application throughout his career. The importance of a leader lies not in his own production but only as he leads people to accomplish their objectives—objectives channeled toward an overall planned result."

The principles I have presented to you today are being carried out by all of you. As responsible members of the hospital team you are devoted to the health profession. So, too, as mature people, you are the people Edward Strecker talks about in his definition of maturity:

"Maturity is a quality of personality made up of a number of elements. It is stick-to-itiveness, the ability to stick to a job, to work on it, and to struggle through it until it is finished, or until one has given all one has in the endeavor. It is the quality or capacity of giving more than is asked or required in a given situation. It is this characteristic that enables others to count on one; thus it is reliability. Persistence is an aspect of maturity; persistence to carry out a goal in the face of difficulties. Endurance enters into the concept of maturity; the endurance of difficulties, unpleasantness, discomfort, frustrations, hardship. The ability to size things up, make one's own decisions, is a characteristic of maturity. This implies a considerable amount of independence. Maturity includes a determination, a will to succeed and achieve, a will to life. Of course, maturity represents the capacity to cooperate; to work with others, to work in an organization and under authority."

Yes, with these essential qualities of maturity your program can only be successful.

AROUND-THE-CLOCK PHARMACY SERVICE

by LOUIS P. JEFFREY

► THERE IS NEED FOR AROUND-THE-CLOCK pharmacy service. By this I mean a registered pharmacist availing himself for duty *continuously* on a twenty-four hour basis. Generally, many pharmacists do not feel that it is feasible, practical, or economical. However, it is essential that the pharmacist extend his services beyond the eight hour work day and beyond the setting up of an emergency night cabinet or press. This twenty-four hour service, I believe, should be the responsibility of a properly qualified pharmacy staff member, not a person whose professional ability and responsibilities lay in other areas.

We will discuss this subject in two phases: First, the situations which create the need for pharmaceutical service during the hours in which the pharmacist is not on duty; Second, how you may provide an extension of these services in your hospital.

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Presented at the Institute on Hospital Pharmacy, Temple University, Philadelphia, Pa., June 1958.

Justification

There are several basic reasons why the services of the Pharmacy Department are required after "5:00 P.M."

1. Late Admissions

When a patient is admitted into the hospital, especially during the latter part of the day, his physician usually makes his initial call late in the afternoon and writes several "orders" which he would like to have started that same day. With the many duties and responsibilities of the nurses at the nursing station—and usually there is a nursing personnel shift at this time—special drug orders are not immediately handled. Therefore, the orders which have not reached the Pharmacy before it closes for the day remain to be filled by some person other than a pharmacist.

2. Physician's hours

As we know, a physician's day, except for office hours, may have no definitely planned schedule. Although his calls at the hospital may follow a routine pattern, usually in the morning, he does visit his

hospitalized patients after office hours, which usually is late in the day or even at night. During his visit, he may write new orders or renew automatic stop-orders. Once again, the need for filling these medication orders occurs during the absence of a pharmacist.

3. Other Departments

There are many other departments in the hospital which provide around-the-clock services: central supply, blood bank, radiology, and hematology. The significance of this is that the medical and nursing services have continuously provided 24-hour service. Therefore, shouldn't we, the Pharmacy Department, accept our share of responsibility on this team by extending our services to a point whereby they will be compatible with the demands of one's institution?

4. Errors

A point not to be over-looked is the human factor of error. Lack of proper information when ordering on the part of hospital personnel responsible for writing out special drug orders, creates an additional problem, *i.e.* not specifying dosage form. The error may then have to be corrected during the hours when the services of a pharmacist are not available. I should like to point out two examples by quoting from the article "You're Not A Pharmacist" by Mary Mac Rostie, R. N. in the nursing journal *RN*.

> "A California nurse ventures this suggestion: 'I think most of my night pharmacy trips could be dispensed with if the day nurse would only check and replenish her supply of ward drugs before the pharmacist goes off duty.'"
> "A Florida R.N. has the same general idea: 'A day nurse can generally anticipate the drug needs of her night nurse. Yet how seldom it's done. I couldn't count the times during the winter months that I've had to go to the pharmacy for analgesic ointment to relieve winter vacationers' sunburns.'"

Methods of Extending Night Service

Emergency Night Cabinet

The use of an emergency night cabinet seems to have been widely accepted by many hospitals as the solution to this problem. I am sure that in some hospitals this arrangement has not only served satisfactorily, but has proven to be the system of choice.

Although this plan is familiar to most of you, I should like to pass along several comments:

(a) The pharmacist at the institution should check with the Department of Internal Revenue and the State Board of Pharmacy, to clarify any legal complications which may exist concerning his responsibilities and liabilities in the storage and dispensing of drugs in such a cabinet.

(b) A night emergency cabinet may not be satisfactory for all drugs. For example, refrigerated items, if there is no refrigerator; narcotics and barbiturates, if they are to be stored.

(c) Dated items should be checked regularly.

(d) The size of the cabinet should be proportionate to the number of items present.

(e) The hazards of permitting unqualified personnel to dispense drugs to hospitalized patients are great.

(f) The most commonly used system is a night cabinet with a pharmacist on call.

The Pharmacy Department

There are several ways in which the proper personnel—ideally a registered pharmacist—may dispense drugs from the Pharmacy and extend pharmaceutical service on an around-the-clock basis.

(a) A pharmacist may be on duty twenty-four hours a day. This, in my opinion, is uneconomical, impractical and not feasible unless the community needs, administrative operation, and unusually heavy requirements of the institution warrant it.

(b) An arrangement whereby the registered staff pharmacists would be "on-call" on a sixteen hour basis. In this instance, I should like to make two reservations. First, that the pharmacist be paid for his on-call time. Second, that he be assigned a room at the hospital if he does not live close enough to the hospital, so that he can report within the time limit for the other professional services that are on call.

(c) In institutions where a hospital pharmacy internship program is established, the after-hour dispensing may be assigned as the responsibility of an intern as a part of his training, providing this has no legal complications.

(d) A registered pharmacist may be on duty for a specified period of time during the evening: for example, 6:00 P.M. to 10:00 P.M. or 7:00 P.M. to 9:00 P.M., in order to fill special drug orders only. This is the type of system that we use at the Albany Hospital. By having such an arrangement, we have filled 83.8 percent (1,328 by pharmacists and 276 by nurses) of the total number of prescriptions sent to the Pharmacy "after-hours." The pharmacist on duty subsequently goes home and remains on call throughout the evening. The evening and night supervisors have available the use of a night emergency cabinet.

Other Methods

I should like to mention several other methods for providing around-the-clock pharmacy service. I am neither advocating nor recommending the adoption of any of these alternatives. They are being presented to you for your consideration.

(a) Some hospitals permit the evening and night nursing supervisors to enter the Pharmacy. The opinion has been expressed, in this case, that the pharmacist is turning over his responsibility to the nurse.

(b) The utilization of a medical resident or intern and placing him on-call for special medication orders.

(c) Coordinate activities by training a registered pharmacist as an evening or night nursing supervisor. Or, possibly obtain a person who is both a nurse and a pharmacist to handle this program.

(d) Place a senior pharmacy student on an on-call basis. I would question the legality of this method.

(e) Form a satisfactory arrangement with a retail pharmacy which is open all night. Is this professionally rewarding?

Summary

The need for providing around-the-clock pharmacy services, I feel sure, is justified in terms of pharmaceutical responsibility, moral principles, and professional ethics. But with the critical shortage of pharmacists, particularly properly qualified hospital pharmacists, it does not appear that a registered pharmacist on duty continuously for twenty-four hours can be justified in terms of economic feasibility or sound practicalities. I believe that the ideal solution is to provide around-the-clock pharmacy service with a registered pharmacist. In my opinion, this could be best accomplished by having limited pharmacy evening hours and a registered pharmacist on call during the hours in which the Pharmacy is not open, plus the use of an emergency night cabinet.

In closing, I should like to leave with you one thought. At the present time, most of us are providing twenty-four hour service with or without a registered pharmacist. If we do not assume the initiative in providing this service, are we serving the patient to the best of our ability? Are we accepting our responsibility as pharmacists?

PAINTING THE PHARMACIST INTO THE PICTURE

by Sir Hugh Linstead

► THOMAS TRAHERNE, AN ENGLISH POET AND MYSTIC, tells each of us that "you never enjoy the world aright till the sea itself floweth in your veins, till you are clothed with the heavens, and crowned with the stars: and perceive yourself to be the sole heir of the whole world, and, *more than so,* because men are in it who are every one sole heirs as well as you."

This is the theme that animates the great exhibition here in Brussels: that man is "the sole heir of the whole world." And not just "man," any man, but you and I, each of us, as an individual: this world is our world. An exhibition with such a theme could not have been held at a more appropriate moment of history. It is my own belief that fear—fear of atomic warfare—has halted humanity on the very brink of annihilation and that from now on we face years of readjustment and reassessment without a major conflict. They will be years during which mankind will need to meet and overcome other obstacles than war that stand in the way of his inheriting the world.

Rich Complication Of Living

Many of these new problems will be created for man by the sheer success of the current scientific revolution. We have all seen the effect of this within the field of medicine to which almost every science has made its contribution of discovery in the past half-century. Essentially, of course, this *embarras de choix* is excellent. But multiplied, as it is in every direction in which we look, such a rich complication of living can overwhelm the individual human being.

The problem for humanity today is therefore how man is to reassert his control over his environment. It is he who builds these bigger, better and faster machines. He puts his sputniks into space. He fills the atmosphere with his radio waves day and night. The bronze age followed the stone age, the iron age followed the bronze age. Now modern man has created the paper age for his own confusion. How is he to find the clue that will lead him out of his man-made maze? To be more limited and more precise, what can we in pharmacy do to keep, or to put back, the individual pharmacist in the center of the pharmaceutical picture?

That is the challenge to us of the theme of Brussels, 1958.

The man-made complications within pharmacy are well enough known to all of us. For an example, there are today in the Library of the Pharmaceutical Society of Great Britain some thirty national pharmacopœias and also the *International Pharmacopœia.* Each of them tells us the solubility of many substances in many solvents, the molecular formulae of many substances, the melting points of many substances. *The International Pharmacopœia* has made an heroic effort to coordinate much of this information and for these efforts

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Excerpts from the opening Address of the President of the International Pharmaceutical Federation, Brussels, 1958.

the pharmaceutical world must be grateful. Yet even its aid is sometimes disdained for what can surely be the most microscopic of reasons. Water, says the *International Pharmacopœia*, is a "clear, colourless, odourless, tasteless liquid." Water, says the *British Pharmacopœia*, is "clear, colourless, tasteless." Water, says the *United States Pharmacopeia* is "clear, colorless, odorless." These national pharmacopœias are prepared by commissions and sub-commissions on which serve professors, pharmacists, physicians, chemists, pharmaceutical manufacturers, and other experts. They are distinguished men who yet take time out of busy lives to serve upon these bodies. Pharmacy in every country is indebted to them. And yet has not the time come for someone to question whether it is necessary in these thirty countries and more, for thirty commissions and more to meet year in and year out in order to inform us that in Britain water is tasteless but not odourless and in the United States odourless but not tasteless?

The road along which we must look for the simplification of these modern problems of ours is international cooperation. In the field of medicine we have the World Health Organization, the World Medical Association and our own International Pharmaceutical Federation at our service.

Very much unnecessary duplication of effort at a national level could be avoided if, for example, the standards of the *International Pharmacopœia* were adopted more readily by national commissions and if a serious attempt were to be made by international agreement to produce an international register of names for new medicaments which would be authoritative in every country.

When we consider the complications created by the increasing use of advertising and propaganda of all kinds in relation to medicines, we can see clearly that there can be one antidote only against the excessive enthusiasm that commends a new medicine to physi-

cians and pharmacists. That antidote must be the scientific knowledge of the physician and the pharmacist. Here, indeed, is the modern rôle of the pharmacist, to keep abreast of the new wealth that pours out from our research laboratories. Then he can offer to the physician that service of which the physician has increasing need, a considered and balanced judgment upon the value of these medicaments, a judicial assessment of the propaganda of the manufacturers. Such an assessment is an essential element in any service for the sick, private or public. It is a service that can be performed only by a most competent pharmacist, equipped with wide scientific knowledge, who also possesses those personal qualities of judgment and integrity which alone can give authority to his opinions.

Pharmacy is both a science and a profession. Pharmacy as a science is concerned with the discovery and preparation of substances for the physician to use in the prevention, cure or relief of illness. Pharmacy as a profession distributes them. Pharmacy as a science can join in the scientific revolution with enthusiasm. Pharmacy as a profession must regard it with respectful caution.

In pharmacy we have all seen the center of gravity shift from the pharmacy to the factory. We know that the specialty is increasingly replacing the extemporaneously prepared medicine. If we allow our imagination to take flight, we can visualize a continuation of this trend to the stage where the choice of a medicine after a diagnosis has been made will be almost mechanical. In such a state of affairs dispensing might become a purely automatic action calling for little more from the pharmacist than the ability to read accurately. No conception of prescribing or of dispensing could be more wrong nor charged with greater danger to the fundamental ideals of the care of sick persons.

We could apply the same line of reasoning to diagnosis. We can imagine the physician receiving from various departments of a hospital reports upon a patient—a radiograph, an electrocardiograph, analyses of blood, urine and sputum, records of blood pressure, and so on. And it is conceivable (provided all the reports related to the same patient) that a sound diagnosis could be made from them. It is even possible that adequate treatment could be prescribed without physician and patient coming into contact. Indeed radio renders just that very thing possible and valuable at sea. And yet in all normal circumstances such a procedure is recognized clearly as a travesty of good medical practice. Why? Because the patient is a human being and not a piece of biochemical apparatus. Because his needs are not to be satisfied solely by mechanical means.

A client comes to a pharmacy. He may not know clearly what is the name of what he is seeking. He may have forgotten the instructions given him by the doctor. He may be trying to treat himself when he should be examined by a physician. He may be a drug addict. He may be under the influence of alcohol. He may be a child who should not be trusted with a dangerous medicine. He may offer a forged prescription. He may be a foreigner with a foreign prescription. He may have a prescription that has been wrongly written. He may come in the middle of the night. He may have come without money. A similar series of problems could be drawn up dealing with the relations between physician and pharmacist. Each of these events presents the pharmacist with a professional problem to be solved according to his professional standards and conscience. None of them is a problem that can be solved mechanically. And, above all, most clients who come for medicines are in some degree in distress and are in need of the indefinable sympathy that can be offered only by an individual whose conception of his duty extends far beyond the mechanical handing over of a package.

Ministries of Health, municipalities, sickness insurance societies, all who are responsible for the organization of services for the sick have a high responsibility for seeing that humanity and personality are not sacrificed to economy or superficial efficiency anywhere in the service. Once the infection of impersonality penetrates a health service it may remain superficially efficient, but it may well have lost its humanity in the process.

The pharmacist has the responsibility and the duty sometimes to say no. He must also have the freedom to say no. To say no to a physician if the interests of a patient seems to demand it. To say no to a client in his own best interests. To say no even to a sickness insurance society or even to a Ministry of Health. He will rarely need to exercise that right. More often he will be aiding and advising the physician, the client, the society or the Ministry. But the right to say no according to professional standards is a right that belongs to every independent professional man because he is independent, because he is a professional man, indeed because he is a man. It is not something to be frowned upon and discouraged by authority. It is something to be encouraged. That way lie the best professional men and that way the best health services.

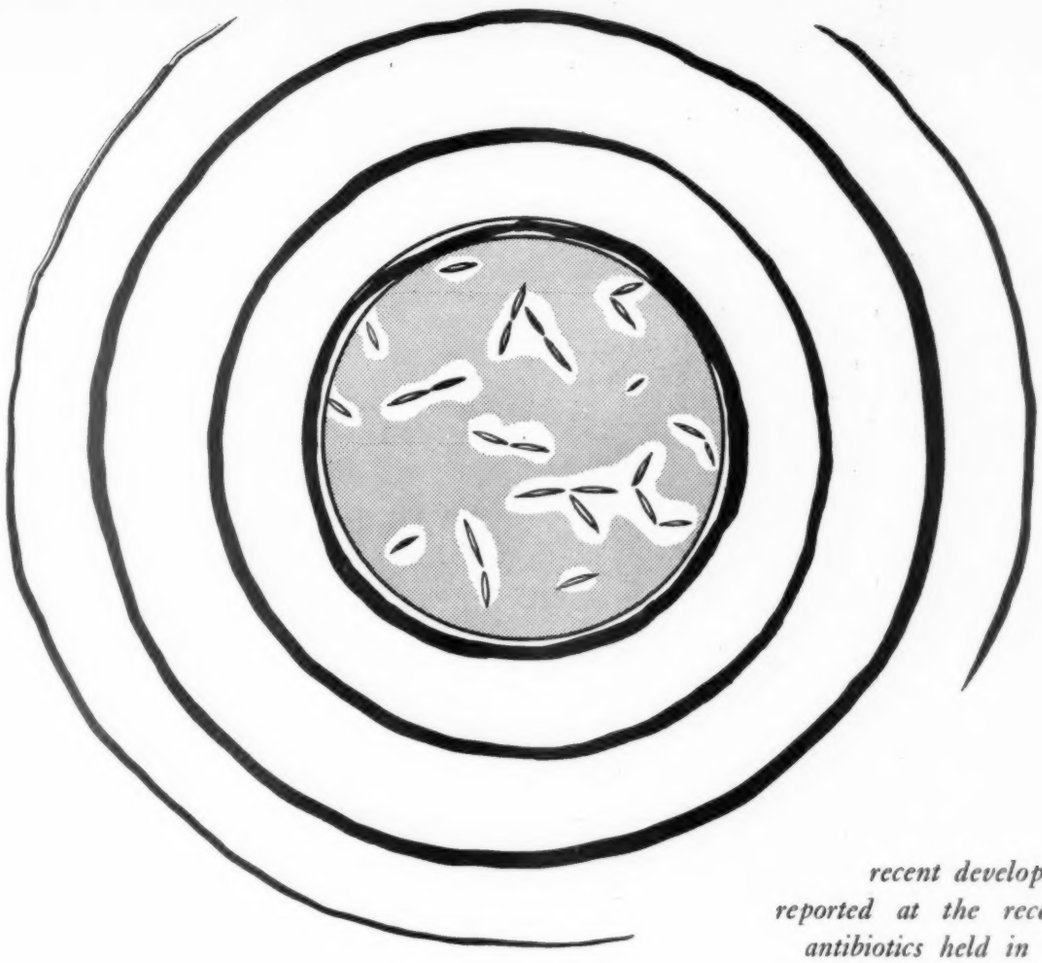
No words are too strong to emphasize the importance of the personal element in dealings with the sick. A British surgeon once said that a hospital would never fully serve its patients until every member of the staff from the most senior surgeon to the most junior porter felt that he had a personal, unwritten contract with each individual patient for their proper care and attention. That same attitude of mind must permeate every level of health service, whether it be a state service or a privately organized service, if it is fully to satisfy the human needs of those who are treated by it.

ANTI BIOTICS TODAY

► THE SIXTH ANNUAL SYMPOSIUM on Antibiotics, sponsored by the Food and Drug Administration in collaboration with the journals *Antibiotics and Chemotherapy* and *Antibiotic Medicine and Clinical Therapy,* was held in Washington, D.C. October 15, 16, and 17. Recent discoveries and advances in the field of antibiotics were reported by leading scientists from the United States and abroad. A total of 181 papers were presented.

Chairman of the Symposium was Dr. Henry Welch, Director of the Division of Antibiotics, Food and Drug Administration, Department of Health, Education, and Welfare.

Because hospital pharmacists are closely associated with medical practitioners, an attempt is made here to present a brief account of some of the subjects discussed. This resume is based on information released by the Food and Drug Administration.



a summary of recent developments in antibiotics reported at the recent symposium on antibiotics held in Washington, D. C.

► ACTINOBOLIN is a new antibiotic obtained from aerated broth cultures of a *Streptomyces*. A report on the origin and biologic evaluation of actinobolin was reported by Pittillo and co-workers. It is a potent inhibitor of various gram-positive and gram-negative bacteria *in vitro*. Relatively high doses protected mice against experimental staphylococcal, streptococcal, and *Klebsiella* infections, but failed to protect against experimental *Diplococcus* and *Proteus* infections. Gram-positive cocci developed resistance to actinobolin *in vitro*, but cross-resistance with the principal clinically employed antibiotics does not occur. Actinobolin inhibits *Plasmodium lophurae* infections in chicks but is only approximately one-tenth as active as quinine. High doses are well-tolerated by mice, rats, dogs, and monkeys. No irritation occurs at the sites of injection and no evidence of significant irreversible organ toxicity has been observed. The antibiotic appears to be poorly absorbed following oral administration. Parenteral doses are followed by substantial but transitory blood levels and sustained high urine levels. The antibiotic is assayed by an agar-diffusion assay using *Sarcina lutea* as the test organism.

According to Haskell and Bartz, microanalyses of the crystalline acetate and sulfate salts of actinobolin support the empirical formula $C_{13}H_{20-22}N_2O_6$ for the free base. The base as well as its salts are extremely water-soluble and cannot be satisfactorily extracted from aqueous solutions with any of the common immiscible organic solvents. The antibiotic is amphoteric and complexes iron III and aluminum quite readily. It has powerful chelating properties.

The effects of actinobolin on transplanted mouse leukemias were reported by Burchenal *et al.* Although the crude filtrate was inactive against sarcoma 180, a purified preparation was found later to be active against this tumor. At 800 mg./Kg. given intraperitoneally daily, the mean survival time in mice injected with leukemia L1210 was increased from 11.3 days in the controls to 20.3 days in the treated mice. Significant prolongation of survival time or inhibition of tumor growth also occurred in leukemias P1081, P388, B82, B82T, and B8174T, but there was somewhat less effect on P329 and P815. Since ferric chloride, aluminum chloride and magnesium sulfate prevented the inhibitory effect of actinobolin on *Streptococcus faecalis*, the effects of various metal ions on the antileukemic action of the antibiotic have been studied in leukemias L1210 and B82T. Actinobolin was equally effective on strains of L1210 sensitive or resistant to amethopterin and mercaptopurine. A line of L1210, originally very sensitive to this compound, was passed through animals treated with actinobolin, 800 mg./Kg. daily. By the 35th generation, resistance was apparently complete, but there was no cross-resistance to amethopterin, diazo-oxo-norleucine, or 5-fluorouracil. These studies on cross-resistance suggest that the antibiotic is acting in mouse leukemias by a mechanism differing from those of previously known antileukemic agents.

Other studies on the effects of actinobolin on tumors were reported by Sugiura and Reilly, Merker and Woolley, and Teller, Merker, Palm and Woolley.

AMPHOTERICIN B in the treatment of systemic fungal infections was described by Utz *et al.* of the U. S. Public Health Service. The effects of amphotericin B administered intravenously were studied in 21 patients with culturally proved systemic fungal infections. Diseases treated included: histoplasmosis (4), cryptococcosis (6), blastomycosis (4), coccidioidomycosis (3), and candidiasis (4). *In vitro* sensitivity of the infecting fungus was determined in 7 cases and the serum antibiotic level measured in 12 patients at a time, 24 hours after infusion of therapeutic doses. The drug was added to 250 ml. of 5 percent solution of glucose in water and given by infusion during a period of 3 to 6 hours. Duration of therapy varied from 10 days to 7 months. Daily dosage was, with the exception of one case, in the amount of 0.3 to 0.75 mg./Kg.

In 2 patients therapy was discontinued before what was considered an adequate course of therapy was given. Eight patients made an apparent recovery from their illnesses with conversion of positive cultures to negative. Appropriate cultures of 3 additional patients became negative and their clinical status improved, although recovery was not judged complete. Four patients were unchanged and 4 additional patients died of their disease. Each of 3 patients with blastomycosis and 3 of 4 histoplasmosis patients given an adequate course of therapy have made apparent recoveries. Two patients with cryptococcosis had no clinical or cerebrospinal fluid signs of illness and 2 others were improved following therapy. No patient with coccidioidomycosis and only 1 patient with candidiasis demonstrated cultural reversal or clinical improvement. Toxic reactions observed were an elevation of the blood urea nitrogen (12 patients), chills or fever following infusion (13 patients), and gastrointestinal symptoms of nausea, vomiting or anorexia (14 patients). No patient was felt to have been free of any side effects.

The use of amphotericin B to eliminate *Candida* from the stools of infants treated with tetracycline was studied by Lepper and his colleagues of the Municipal Contagious Disease Hospital in Chicago. It was concluded that at least 10 mg./Kg. should be used to control *Candida* in the stools of infants when this is desired.

The development of strains of *Candida albicans* and *Coccidioides immitis* which are resistant to amphotericin B was discussed by Sorensen *et al.* of the University of California Medical Center in Los Angeles. Three strains of *Candida albicans* and two strains of *Coccidioides immitis* became resistant to amphotericin B by continual passage in media containing gradually increasing increments of this antibiotic. Two of the *Candida albicans* strains were not completely inhibited by 1000 ug./ml. of amphotericin B although partial inhibition was observed at lower levels. When these amphotericin B resistant strains were tested against their susceptibility to nystatin and pimaricin, cross-resistance was evident when nystatin was used, but not when pimaricin was used. This cross-resistance assumes clinical significance since both amphotericin B and nystatin are used for the therapy of candidiasis.

BACITRACIN-NEOMYCIN DETERGENT SPRAY was studied for its effectiveness in the treatment of massive experimental wounds by Knecht *et al.* of the Chemical Warfare Laboratories, Army Chemical Center in Maryland. Employing goats subjected to a uniformly lethal massive hind leg injury, it was found that local bacitracin-neomycin detergent spray therapy, alone or in conjunction with intramuscular penicillin, suppressed all the major components of the wound flora. The efficacy of local bacitracin-neomycin spray and the ineffectiveness of intramuscular bacitracin-neomycin therapy confirmed previous studies which point to the wound as the site of detrimental bacterial action in this wound shock preparation. The effectiveness of this preparation when sprayed into the remote recesses of the wound and around damaged tissue with impaired circulation suggests its possible clinical application in the treatment of mass casualties.

The enhancement of bacitracin by metallic ions of Group II B was reported by Weinberg of Indiana University. The test bacteria consisted of strains of *Staphylococcus aureus*, *Bacillus subtilis*, and *Escherichia coli*. With each test strain salts of zinc strongly enhance the action of bacitracin. Moderate enhancement is obtained with salts of cadmium and mercury. With gram-positive strains, salts of aluminum and cobalt slightly enhance the antibiotic. Salts of no other metallic ions affect the drug. Of the metal binding agents, ethylenediamine tetraacetate (EDTA) and cyclohexanediamine tetraacetate strongly suppress bacitracin. Differences of as much as 450-fold in the antibacterial activity of bacitracin can be obtained merely by including in nutrient agar or broth concentrations of salts of zinc or EDTA which, in themselves, have no apparent effect on the growth of the bacteria. It is suggested that, in addition to enhancing the thermal and storage stability of the drug, zinc is also associated with the mechanisms of antibacterial and nutritional action of bacitracin.

ERYTHROMYCIN PROPIONATE was the subject of several reports presented by workers at the Lilly Research Laboratories and the University of Washington School of Medicine. Comparative studies *in vitro* indicate the spectrum and potency of erythromycin propionate, expressed as erythromycin base, are equivalent to those of erythromycin base. Blood level studies show an earlier onset of therapeutic concentration with the capsules of erythromycin propionate than with the tablet protected by an acid-resistant coating. Serum levels with the propionate are significantly higher than those with the base, either in acid-resistant tablets or in capsules. The levels with the propionate also last longer than those with the coated tablet or capsules of the base. Toxicity studies indicate no evidence of toxicity or severe side effects. Erythromycin propionate was used in a dosage of 250 and 500 mg. every 6 hours to treat infections caused by organisms in the spectrum of erythromycin. Results indicated that erythromycin propionate is effective in rapidly controlling susceptible infections.

Perry and co-workers at the University of Washington School of Medicine found that erythromycin serum concentrations were significantly higher (greater than 100 percent) with capsules of erythromycin propionate than with the coated tablets of erythromycin base. These workers concluded that the propionate should supplant erythromycin base for clinical therapy.

Lee and co-workers at Lilly Research Laboratories found that rats excreted the antibiotic in the bile to a greater degree following administration of erythromycin base than after administration of the propionate. Large doses of the propionate, both by intravenous and intraduodenal administration, were followed by a slight and transient fall in blood pressure and an increase in intestinal motility. This was also observed with erythromycin base.

Erythromycin ethyl succinate was investigated following intramuscular injection by Metzger *et al.* of Cook County

Hospital, Chicago. Intragluteal injections of 100 mg. of the drug in adults (29) or 50 mg. in children (20 studied) resulted in rapid absorption and maintenance in many individuals of measurable concentrations in the blood for at least 12 hours. Fifty-five adult patients with acute infections were treated and in 45 the response was rapid. The infections that did not respond were due mainly to erythromycin-resistant organisms or to gram-negative organisms. A dosage of 100 mg. intramuscularly each 12 hours was effective and local discomfort due to the injection was minimal. The authors suggested that this form of erythromycin should prove valuable in the treatment of acutely ill patients with gram-positive types of infections and perhaps especially with staphylococcal infections.

FUMAGILLIN is an antibiotic isolated from a strain of *Aspergillus fumigatus*. Studies on the carcinolytic activity of fumagillin and some of its derivatives were reported by DiPaolo *et al.* of the Roswell Park Memorial Institute, Buffalo, New York. Eight alcohol moieties, all containing a methoxy group and an unsaturated dicarboxylic acid side-chain, were contributed by Tarbell. As a result of preliminary screening with *B. subtilis* 6051 (disc assay-agar technique), alcohol-I, which contains an epoxide group, dihydroalcohol-Ib, made by reducing the alcohol-I to a diol, and the unsaturated acid were tested for their tumor-inhibiting properties. These chemicals and fumagillin were tested by agar tests containing Ehrlich ascites cells and on the following mouse tumors *in vivo*: Sarcoma 180, carcinoma C-755 and C3HBA, leukemia 1210, Krebs-2 ascites and solid, and Ehrlich-2 ascites. The animals were given intraperitoneal injections twice daily for 7 or 14 days, commencing the day following tumor implantation. At a concentration of 30 mg./Kg. all tumors showed some response to fumagillin. Survival time of the mouse ascites tumors was extended 50 percent while the solid tumors were ⅓ to ½ the size of the controls. The unsaturated side-chain has been used at concentrations varying from 125 to 500 mg./Kg. Thus far, only C-755 has been inhibited 35 percent at a concentration of 125 mg./Kg. No inhibition of growth has been noted with the other tumors. Of the two alcohols, alcohol-I proved to be the better carcinostatic compound. Tumor inhibition as great as 85 percent was obtained with 25 mg./Kg./day. No carcinostatic activity was noted in human beings with fumagillin itself. The effects of alcohol-I on dogs and preliminary results on patients were presented.

GAMMA GLOBULIN in combination with antibiotics was the subject of several reports. Schonholtz *et al.* of the Walter Reed Army Medical Center reported on the use of gamma globulin with chloramphenicol (17 cases) or novobiocin (2 cases) in the treatment of various forms of active osteomyelitis. The response to therapy was considered excellent in 10 cases, good in 2 cases, fair in 2 cases, and poor in 5 cases. Of 12 patients who responded to chloramphenicol and gamma globulin therapy, 9 had an adequate prior trial of chloramphenicol alone, without response.

The combined use of chloramphenicol and gamma globulin therapy in the treatment of lymphogranuloma venereum was reported by Loughlin *et al.* of the New York Medical College and Flower and Fifth Avenue Hospitals. In all cases the dosage of the antibiotic was 1 Gm. daily for 7 days. The dose of gamma globulin was a single dose of 10 ml.; however, in the majority of cases this was followed by a second dose of 10 ml. on the fourth day of therapy. Results of the therapy were considered excellent and none of the patients, all of whom have been observed for periods of 7 to 12 months, have relapsed.

KANAMYCIN and its clinical use was the subject of several papers presented. Kanamycin sulfate, an antibiotic of Japanese origin produced from *Streptomyces kanamyceticus*, has a broad spectrum of activity against both gram-positive and gram-negative organisms. The absorption of the antibiotic after oral administration is negligible, but human serum levels comparable to *in vitro* inhibitory concentrations can be achieved following the intramuscular administration of the drug.

Finegold and co-workers, at the V.A. Hospital and the University of California Medical School, treated more than 100 patients with kanamycin administered parenterally. Most of these patients had staphylococcal infections; various gram-negative bacillary infections and a few pneumococcal infections were also treated. Response was good to excellent, but there were several failures. For example, *Bacteroides* infections did not respond and kanamycin is not considered indicated for pneumococcal infections; *Pseudomonas* infections sometimes respond but are often resistant. The drug was usually given intramuscularly but was well-tolerated intravenously in a few patients. Major toxic manifestations were eighth nerve and renal damage. Renal damage was more common in older patients and was important only as it predisposed to eighth nerve damage. Auditory or vestibular damage was clearly related to either larger doses or prolonged therapy, or both; such damage was also more common in patients with pre-existing or kanamycin-induced renal damage. Impaired hearing is not necessarily bilateral, complete, or permanent and does not appear to be progressive over long periods of time. Tinnitus is often an early sign of eighth nerve damage. The authors treated 10 patients with oral kanamycin for either intestinal antisepsis or treatment of Salmonellosis and the results were excellent.

A critical clinical evaluation of kanamycin in severe infections was carried out by Duke *et al.* at the District of Columbia General Hospital. Cases reported on included endocarditis, purulent meningitis, septicemia, pyogenic arthritis and osteomyelitis, septic endometritis, lung abscess, and pneumonia. The bacterial agents implicated in this list were predominantly *M. pyogenes* var. *aureus* and organisms of the *Proteus* species. Kanamycin proved to be generally effective in the patients studied. In several instances, it was considered to have been life-saving, as in the case of staphylococcic endocarditis. Significant toxicity was noted in 2 patients.

The use of kanamycin in genitourinary infections was reported by Dougherty and Seneca of the Squier Urological Clinic in New York. The drug was administered intramuscularly in doses of 0.5 Gm. every 6 hours for an average of 6 to 7 days (range 4 to 18 days). In conclusion, the authors stated that kanamycin is highly effective against *A. aerogenes* and *E. coli* genitourinary infections but has a low grade activity against *Pseudomonas* and enterococcus infections. The renal toxicity does not appear to contraindicate its use for kanamycin-sensitive genitourinary infections in the presence of impaired renal function. The auditory nerve toxicity is significant and should limit the use of kanamycin solely to susceptible infections in patients who have had no previous auditory damage and in doses of about 30 mg./Kg. per day for approximately 7 days.

Observations on the treatment of acute gonococcal urethritis in the male with intramuscular kanamycin were reported by Marmell and Prigot of Harlem Hospital, New York. The most satisfactory response was obtained when 1 Gm. of kana-

mycin was given intramuscularly daily for three days. This resulted in a cure rate of more than 90 percent. No toxic or allergic manifestations were noted.

A study to determine the effectiveness of kanamycin in the treatment of chronic pulmonary infections in a total of 13 patients with fibrocystic disease of the pancreas was reported by Huang, Serria, and High of Temple University School of Medicine. All patients received kanamycin by intramuscular injection and concurrently by aerosol inhalation. The intramuscular dose varied from 20 to 60 mg./Kg. per day divided into two doses. The aerosol dose varied from 100 to 250 mg. for each treatment. Clinical results were good in 7 patients and fair in 6. Long-term aerosol therapy using kanamycin in a dosage of 250 mg. three times daily for as long as two months has not shown any adverse effects.

Use of kanamycin in pediatric infections was discussed by Thurman and Platou of the Tulane School of Medicine. The drug was used in 144 cases of pediatric infections having varying etiologies. It was found efficacious in the therapy of enteric infections (*Salmonella, Shigella, E. coli*), superficial skin infections (staphylococcal, streptococcal), and, most importantly, to be bactericidal against many resistant staphylococcal infections. The authors concluded that kanamycin is an effective and important addition to present therapeutic agents. In their experiences toxicity was not a deterrent when therapeutic regimens were carefully planned and controlled.

Use of kanamycin in staphylococcal and other infections of infancy and childhood was discussed by Riley of the University of Oklahoma Medical Center. Thirty-two patients ranging from 3 days to 15 years in age with infections due to a wide variety of bacterial agents were treated with kanamycin. Disease entities included pneumonia, empyema, septicemia, pyoderma, tularemia, bacillary dysentery, gastroenteritis, pharyngo-tonsillitis, pertussis, pyelonephritis, and suppurative otitis media. Of the 13 patients with infections due to *Staphylococcus aureus,* 4 had pneumonia, 2 empyema, 1 gastroenteritis, 2 septicemia, and 4 pyoderma. Most organisms were resistant to the commonly employed antimicrobial agents. However, all staphylococcal strains tested by tube dilution method were susceptible to kanamycin in a concentration of 5 ug./ml. or less. Initially a dose of 15 mg./Kg. per day for no longer than seven consecutive days was utilized. Later, in more severe infections, doses of 50 to 75 mg./Kg. per day were employed. Cylinduria occurred intermittently on some of the higher doses but was reversible on discontinuing therapy. Results of kanamycin therapy were in general good in children with staphylococcal infections. Failures could be attributed primarily to late institution of therapy.

The effect of kanamycin on the intestinal microflora of man was reported by Shidlovsky and Prigot of Harlem Hospital. The most satisfactory results were obtained when 4 Gm. of kanamycin was administered in four divided doses in one day. Bacteriological cultures revealed a significant reduction in colonies of the total aerobic microbial population of the intestines and in the gram-negative and the staphylococcal counts approximately 24 hours after termination of medication. The drug was well-tolerated and no side reactions were observed.

Use of kanamycin in the treatment of chronic amebiasis, brucellosis, and other infections was reported by Sanchez *et al.* of Guadalajara, Mexico and White *et al.* of Vanderbilt University. Amebic cysts were eliminated from the stools of 36 of 41 carriers treated by the oral route. Two patients with acute amebic colitis improved promptly with treatment. Kanamycin intramuscularly was not effective in brucellosis, typhoid, and *Pseudomonas* infection but was beneficial in staphylococcal and *Proteus* infections.

Results with the topical use of kanamycin in superficial pyodermias was reported by Russo of Albany, New York. The author concluded that kanamycin ointment and cream in superficial pyodermias is effective in about the same degree as neomycin.

Kanamycin in the treatment of tuberculosis was the subject of reports by Weiss *et al.* of Philadelphia General Hospital, Frost *et al.* of N.Y. University-Bellevue Medical Center, and by Shapiro and Hyde of the V.A. Hospital and the University of California Medical School at Los Angeles. Shapiro and Hyde gave kanamycin intramuscularly in doses of 1 Gm. daily for the first 28 days and thereafter 1 Gm. three times a week. In their series they used 39 cases of chronic pulmonary tuberculosis regarded as treatment failures and kanamycin was added to their previous antituberculous chemotherapeutic regimens. The authors concluded that the use of kanamycin merits consideration as adjunctive therapy in pulmonary tuberculosis but stated that it is too early to evaluate its precise role. Although 85 percent and 46 percent of patients developed urinary casts and proteinuria, respectively, kanamycin therapy was continued and produced no increase in these findings.

Results of studies reported by Weiss, *et al.* suggest that kanamycin has a lower order of efficacy and a significant toxicity in the treatment of pulmonary tuberculosis. Dosage used was 1 Gm. intramuscularly daily.

Frost *et al.* concluded that the cochlear toxicity of kanamycin appears to be too severe to permit prolonged use in a dose of 1 Gm. (or 20 mg./Kg.) daily in the treatment of tuberculosis.

Intraperitoneal administration of kanamycin was the subject of a paper by Cohn of the Louisiana State University School of Medicine. Various concentrations of kanamycin, neomycin, and tetracycline were given intraperitoneally to normal rabbits and to normal and anesthetized dogs. Tetracycline was associated with pain on injection. A fatal result was observed when large doses of neomycin or tetracycline were used. In smaller doses, adhesions were produced. Kanamycin was associated with neither local nor systemic effects and was well-tolerated in large doses (up to 5 Gm. in a 10 percent solution). The author concludes that neither neomycin nor tetracycline is as safe for intraperitoneal administration as is kanamycin.

Studies on the mechanism of action of kanamycin were reported by Gourevitch *et al.* of Bristol Laboratories. Kanamycin is more active under conditions of higher than lower oxygen tension. Acids of the Krebs citric acid cycle protect bacterial cells from kanamycin damage, while related compounds, like glutamic acid, do not. Complex organic nutrients, like peptones, and yeast extract, also protect. Human serum, on the contrary, is inactive. The data are interpreted to indicate that kanamycin produces a biochemical lesion in the oxidative respiratory system.

A comparison of kanamycin and kanamycin B was the subject of a presentation by Tisch *et al.* of Bristol Laboratories. Kanamycin B, the second antibiotic isolated from fermentations yielding kanamycin, is twice as potent and at least two to three times more toxic acutely than kanamycin.

LEUCOMYCIN was discussed by Welch *et al.* of the Food and Drug Administration and by Steinberg *et al.* of The Wm. S. Merrell Company and The J. T. Baker Company. Leucomycin is a new antibiotic discovered in Japan by Hata. It is said to be identical with the antibiotic labeled C-637. Leucomycin has been reported active mainly

against gram-positive organisms and a few gram-negative ones. Welch *et al.* tested 47 cultures, representing seven genera, for their susceptibility to leucomycin. For comparison the same organisms were tested for susceptibility to erythromycin and kanamycin. In addition, 201 cultures of coagulase-positive *Staphylococcus aureus* were tested for susceptibility to leucomycin and penicillin; 168 of these were tested against erythromycin; 133 against chloramphenicol, novobiocin, oleandomycin, streptomycin, and tetracycline; and 78 against kanamycin. Leucomycin was not active against the organisms of the genera *Aerobacter, Escherichia, Proteus, Pseudomonas, Salmonella,* and *Shigella.* The same held true for erythromycin. Leucomycin and erythromycin were very active against the streptococci, while kanamycin was relatively inactive. Kanamycin was moderately active against *Proteus, Salmonella,* and *Shigella* cultures, only slightly active against *Aerobacter* and *Escherichia,* and almost inactive against *Pseudomonas* organisms.

Of the 200 *Staphylococcus aureus* cultures tested, 193 were inhibited by leucomycin in quantities of 1 ug./ml. or less and three by 2 ug./ml. or less. Four cultures were leucomycin-resistant. Ninety-three of the 200 cultures were resistant to from 1 to 5 antibiotics each, and 80 were penicillin-resistant. Thirty-four of the 178 cultures were erythromycin-resistant. Of the 133 cultures, 4 were oleandomycin-resistant, 55 were streptomycin-resistant, and 58 were tetracycline-resistant. All 78 cultures tested against kanamycin were susceptible, as were the 133 tested against chloramphenicol and novobiocin. Of the 4 leucomycin-resistant cultures, 2 were penicillin-resistant, all were resistant to erythromycin, oleandomycin, streptomycin and tetracycline, and all were susceptible to chloramphenicol, kanamycin and novobiocin. The authors state that leucomycin should be of particular value in combating infections due to *Staphylococcus aureus* resistant to other antibiotics.

Leucomycin is absorbed from the gastrointestinal tract. It appears to be relatively nontoxic.

M5-18903 is a new antibiotic related to aburamycin. Gale and co-workers of Eli Lilly report that an unidentified species of *Streptomyces* will yield a weakly acidic antibiotic effective against mycobacteria and gram-positive organisms. M5-18903 increases the survival time of mice infected with leukemia P-1534. The active substance could be isolated by extraction with chloroform and could be purified by chromatographic procedures and obtained in crystalline form. An evaluation of physical and chemical properties of this antibiotic shows it to be identical with aburamycin with the exception of a variation in its specific rotation.

MITOMYCIN C was discussed by Shiraha and colleagues of the Osaka University Medical School, Japan. Hata *et al.* first reported that mitomycin, a new antibiotic isolated from broth cultures of *Streptomyces caespitosus,* is active against gram-positive and gram-negative bacteria and also possesses strong antitumor effects on Yoshida ascites sarcoma and Ehrlich carcinoma, both in ascitic and solid forms. Wakaki *et al.* isolated a new active principal in crystalline form, tentatively called mitomycin X and later renamed mitomycin C, of which antitumor activity has been confirmed by a series of experimental studies both in Japan and in the United States.

The authors have treated 82 patients with advanced malignancy by intravenous injection of mitomycin C (64), intra-arterial administration (18), and direct infiltrative injection into the tumor tissue (4). Following clinical use of mitomycin C, regression of tumor, including complete disappearance, was the most remarkable change, accompanying general improvements as indicated by activity and weight gain, reduction of ascites, increase of urinary secretion, amelioration to complete relief of pain, nausea and vomiting.

Mitomycin treated patients developed leukopenia (84 percent in intravenous group and 67 percent in intra-arterial group). However, some of the patients showed no changes of the peripheral blood or developed hyperleukocytosis. Other toxic effects were also experienced (16 percent in the intravenous group and 11 percent in the intra-arterial group) indicated by anorexia, fever, general fatigue, and slight petechiae. This leukopenia could be easily recovered; following intra-arterial administration, the patient almost always completely recovered within 3 weeks without remarkable changes in findings of laboratory examinations. The authors conclude that mitomycin C might be promising as an antitumor antibiotic and would like to emphasize its intra-arterial use through polyethylene tube indwelt in the artery to facilitate therapeutic effects and prevent toxicity.

NITROFURANS, specifically furazolidone and furmethonol, were the subject of three papers. Shidlovsky and Prigot of Harlem Hospital presented data on the effect of furazolidone used alone and in combination with neomycin on the aerobic intestinal microflora of man. Furazolidone was employed alone in two dose schedules, 800 mg. and 1,600 mg. in four divided doses in one day. Neomycin was also used alone, 4 Gm. being given in four divided doses. The combination of neomycin with the higher dosage schedule of furazolidone was also studied. Both the nitrofuran and the antibiotic were well-tolerated by patients at the dosage levels under investigation. Bacteriological studies of stools of patients receiving medication demonstrated that the higher dose schedule of furazolidone afforded a significant reduction in the total bacterial counts and a decrease in the gram-negative and gram-positive organisms and the yeasts and fungi. The combination of furazolidone with neomycin produced a significantly greater reduction in the gram-positive aerobic bacteria than either drug alone.

The nitrofuran furmethonol was the subject of a report by Kefauver *et al.* of Eaton Laboratories. Furmethonol is a potent, bactericidal agent against certain bacterial species including *Staphylococcus, Vibrio, Bacillus, Diplococcus,* and *Escherichia.* One hundred clinical isolates of *Staphylococcus aureus* were sensitive *in vitro* to furmethonol within the range of 2.9 to 8.6 ug./ml. No cross-resistance between the nitrofuran and antibiotics could be shown. Furmethonol was shown to be immediately bacteriostatic to staphylococci with a bactericidal effect within 2 to 4 hours depending upon the drug concentration employed. Mice infected intravenously or intraperitoneally with *Staphylococcus aureus* were cured by low doses of orally or intravenously administered furmethonol.

NOVOBIOCIN in the treatment of staphylococcal surgical infections was discussed by Greenberg *et al.* of the Beth Israel Hospital and Harvard Medical School, Boston. One hundred and thirty consecutive patients with infections of the soft tissues, the extremities in patients with occlusive vascular disease, pulmonary infections, and various other surgical infections due largely to strains of hemolytic staphylococci resistant to other antibiotics, received novobiocin. The drug was effective in the control of infections that had failed to respond to other antibiotics and was particularly useful in the treatment of hospital acquired staphylococcal infections. Novobiocin could be given orally or intravenously, yielding plasma concentrations higher than the *in vitro* bactericidal titer required to inhibit most staphylococcal strains. The clinical response showed a close correlation with the

results of the *in vitro* sensitivity tests. Novobiocin was well-tolerated, and there were no serious systemic reactions.

NYSTATIN, and other antibiotics, employed as dusting powders in candidial and noncadidial diaper rashes was the subject of a paper of Kozinn *et al.* of Maimonides Hospital, Brooklyn. Twenty-eight young children with cutaneous candidiasis and 42 children with persistent or recurring diaper rashes of nonmycotic etiology were treated for 15 days with one of three dusting powders, designated powders A, E, and C, respectively. Powder A contained three percent nystatin-neomycin-gramicidin; powder E contained 100,000 units of nystatin/Gm.; and powder C was an unmedicated talcum powder serving as a control. The composition of the powders was made known to the investigators after completion of the study. Cutaneous candidiasis responded with good to marked improvement to both medicated powders, but showed a high rate of failure with nonmedicated talcum powder control. These findings illustrate the necessity for specific antimycotic therapy in diaper rashes due to *Candida albicans*.

Noncandidial diaper rashes showed slight improvement with all three powders, but the over-all response was somewhat better with the medicated than with nonmedicated preparation. No allergic or inflammatory response attributable to the medication was seen. It is concluded that the medicated powders are of value in the treatment of proven or suspected cutaneous candidiasis and may also be substituted safely for ordinary talcum powder in diaper rashes of nonmycotic etiology.

OLEANDOMYCIN and TRIACETYLOLEANDOMYCIN were the subjects of several presentations.

The correlation of sensitivity patterns of oleandomycin and its clinical effectiveness was reported by Leming and Flanigan of the University of Tennessee School of Medicine. Data was presented on sensitivity patterns of oleandomycin based upon results obtained with over 30,000 sensitivity discs. Clinical results were included on patients who received oleandomycin to correlate *in vitro* sensitivity with *in vivo* response. The study includes a general sensitivity pattern of 500 consecutive cultures with oleandomycin sensitivity discs. A review was presented of all gram-positive cocci on which oleandomycin sensitivity studies were performed. The total number of cultures exceeded 2,500 of which approximately 2,200 were gram-positive cocci. Results indicated that oleandomycin is effective against 97 percent of gram-positive cocci and 94 percent of coagulase-positive hemolytic *Staphylococcus aureus*.

The sensitivity of *Micrococcus pyogenes* to the action of oleandomycin was reported by Rivera *et al.* of the Brooke Army Medical Center. In a series of 143 penicillin-resistant strains of *Micrococcus pyogenes (Staphylococcus aureus)* isolated from burned patients, 98 percent proved to be sensitive to as little as 2 ug. of oleandomycin contained in a commercial disc preparation. No antibiotic synergism was apparent when an oleandomycin-tetracycline wet disc preparation was used compared with oleandomycin alone. The ability of oleandomycin-tetracycline to retard the emergence of resistant variants in 3 of 8 *Micrococcus pyogenes* strains chosen at random, as compared with their rapid development of antibiotic resistance to oleandomycin alone, was demonstrated.

Oleandomycin-tetracycline combination was employed by Pagola *et al.* of Children's Hospital, Mexico City, in the treatment of epidemic typhus. Dosage schedule for the antibiotic combination was 50 mg./Kg. of body weight/day, at 6 hour intervals, for 5 days. In some cases, when symptoms were less severe, therapy was administered for 1 to 3 days, and in one case the patient was given the drug for 7 days. Symptoms disappeared in 2 to 3 days in all cases, and temperature became normal after 36 to 84 hours. In one patient fever lasted for 108 hours.

Oleandomycin-tetracycline combination was used by Schenone of the University of Montevideo, Montevideo, Uruguay, in the treatment of 30 recalcitrant urogenital infections due to the following organisms: *Staphylococcus albus* and *Staphylococcus aureus, Proteus,* pyocyaneus, *E. coli,* corynebacteria, and aerobacteria. In 14 of these cases, therapy with various other antibiotics and sulfonamides had previously proved ineffective. Average daily dosage of the antibiotic combination ranged from 1.0 to 1.5 Gm. Therapeutic response in the 30 patients was rated as follows: excellent 12; satisfactory 14; fair 2; and no response 2.

Oleandomycin-tetracycline combination was used by Arneil of The Royal Hospital for Sick Children, Glasgow, Scotland, for the treatment of acute respiratory infections in 50 children. The author stated that the combination is highly effective in a variety of infections of the respiratory system, being successful in 88 percent of the children.

Oleandomycin-tetracycline combination was used both prophylactically and therapeutically in buccal surgery by Durrieu *et al.* at the School of Odontology, Buenos Aires, Argentina. Dosage ranged from 1 capsule every 6 hours for 5 days when the combination was used prophylactically to as many as 6 capsules every 6 hours when severe chronic infection was present. Of the total of 97 patients, the results were: 90 excellent, 6 good; and 1 poor.

The use of oleandomycin-tetracycline in the therapy of

amebiasis, lymphogranuloma venereum, yaws, tropical ulcer, and acute gonococcal urethritis was reported by Loughlin and co-workers. The high degree of effectiveness of the combination in the treatment of these infections, as reported previously, was maintained. This was especially evident in the results obtained in the treatment of chronic intestinal amebiasis, 82 of 86 patients were cured, and in acute gonococcal urethritis with only one apparent failure among 54 cases.

Rebolledo and Heredia of the General Hospital in Mexico City reported studies on the use of oleandomycin-tetracycline in the treatment of various infectious diseases. Approximately 60 percent of the cases were classified as infectious diarrheas caused by *Shigella, Salmonella,* and *Coliformis.* The rest of the cases consisted of bacterial pneumonias, dermatologic infections, puerperal fever, peritonitis, and others. The intravenous route was used in severe cases while the oral route was used in others. Results were judged satisfactory in approximately 95 percent of the cases.

PENICILLIN and its value as a postoperative prophylaxis was discussed by Sanchez-Ubeda *et al.* of St. Vincent's Hospital and New York University College of Medicine. The author reported 511 cases in the period 1956 to 1958. They show that incidence of infectious complications in general surgical cases would not be affected by the administration of penicillin and streptomycin postoperatively on a routine basis. Although this study demonstrated no serious complications or increased incidence of infections in the treated group, the wide use of penicillin without proper indication has paralleled the generation of hemolytic *Staphylococcus aureus* penicillin-resistant infection in hospital populations. In conclusion, the authors stated, caution should be exercised before initiating prophylaxis with other antibiotics that may at present be considered to be effective against the *Staphylococcus,* until there is clear-cut evidence that general surgical patients will be benefited by it.

The use of "all purpose" penicillin in the treatment of gonorrhea was discussed by Willcox of St. Mary's Hospital, London. It is believed that the gonococcus is becoming less sensitive to penicillin. There is a need to use a penicillin preparation providing peaks of penicillinemia higher than those obtained with repository penicillins. A mixed penicillin containing 300,000 units of crystalline potassium penicillin, 300,000 units of procaine penicillin G, and 600,000 units of benzathine penicillin was used on 95 men. The failure rate was 9.8 percent in Negroes and 5.6 percent in other patients.

PENICILLIN V and its oral utilization was discussed by Berlin and Brante of the Central County Hospital, Eskilstuna, Sweden. Four types of penicillin V were given as rapidly disintegrating tablets to 12 healthy subjects: (1) penicillin V acid, large crystals (100 to 200 μ); (2) penicillin V acid, fine crystals (5 to 10 μ); (3) penicillin V potassium; and (4) penicillin V calcium. Each preparation, 250,000 units was given on a fasting stomach one-half hour after a standardized meal. Plasma levels and urinary recovery were determined in all eight series. All preparations gave a lower peak but significantly longer duration after a meal than on a fasting stomach. The longer duration makes dosage after a meal preferable. When given after a meal, the four preparations differ little. A slightly shorter duration of the potassium salt is not statistically significant. On a fasting stomach the salts (K and Ca) give a significantly higher peak than the acid. The differences are greatly eliminated after one hour. Urinary recovery was 22 to 26 percent in all series, except for the salts on a fasting stomach, where 32 to 34 percent were found. Considering the shorter duration after doses on a fasting stomach, the practical importance of this is questionable. No difference in blood levels or urinary recovery was found between large and fine crystals of penicillin V acid.

PENICILLINASE and its *in vitro* inhibition by various compounds of chemotherapeutic potential was the subject of a report by Sallman and Streitfeld of the University of Miami. If a penicillinase inhibitor were found that could be concentrated in the body to an effective but nontoxic level, it is possible that penicillin, given simultaneously with the inhibitor, would once more prove to be an effective controlling agent of penicillin-resistant staphylococcal disease. To this end, various compounds of chemotherapeutic potential were tested *in vitro* for their ability to inhibit a penicillinase preparation from a penicillin-resistant, disease-producing strain of *Micrococcus pyogenes* var. *aureus.* It was found that trypsin, chymotrypsin, and quinacrine were sufficiently active to warrant *in vivo* study.

PHENYL PARA-AMINOSALICYLATE was discussed by Cohen of the Glen Lake Sanatorium, Oak Terrace, Minn. He compared the tolerance, absorption, and clinical effects of various forms of para-aminosalicylic acid. Preliminary results indicate that phenyl PAS is well tolerated, even on the empty stomach, and is quite comparable in that regard to the acid-resin complex. Previous studies had indicated that the acid-resin complex was tolerated with least difficulty and was superior to other salts of PAS. Serum blood levels of phenyl PAS indicate 2.6 mg. percent at one hour, 3.5 mg. percent at two hours, 2.3 mg. percent at three hours, and 1.6 mg. percent at four hours.

RISTOCETIN is an antibiotic composed of fractions, A and B, both of which demonstrate inhibitory properties essentially against gram-positive bacteria and mycobacteria. A study of the efficacy and toxicity of ristocetin in 20 unselected severe respiratory infections was reported by Billow *et al.* of Harlem Hospital, New York. Daily dosage by intravenous administration was 1.5 to 2 Gm. and treatment ranged from 4 to 7 days. Side reactions during therapy were of short duration, all patients reverting to normal in 3 to 7 days after termination of medication. One patient had generalized macular rash and another complained of chills and vomiting. Transitory hematologic changes were demonstrated in 2 cases of thrombocytopenia and one of leukopenia. The therapeutic response was excellent in 14 of 20 patients. Defervescence and decrease in toxicity was prompt and resolution of pneumonic processes was demonstrated by roentgenograms.

The use of ristocetin in staphylococcal infections was reported by Bush of the Geisinger Memorial Hospital and Foss Clinic of Danville, Pa. In all but 2 instances, ristocetin was used in the treatment of gram-positive staphylococci. In the 2 instances in which it was used in the hemolytic streptococci, it seemed less effective. The predominating organism was the hemolytic *Staphylococcus,* coagulase-positive, all of which had phage typing, and all of which had the sensitivity tests in the laboratory. In all but 2 cases, the results of the treatment by ristocetin aided not only in the patient's recovery but were felt highly satisfactory by the physicians using the drug.

The use of ristocetin in a case of staphylococcal meningitis was reported by Kanner of Lexington, Ky. Hemolytic *Staphylococcus aureus,* coagulase-positive, was identified and, by disc tests, was sensitive to the usual antibiotics. Treatment began with penicillin, erythromycin, and corticoids. Streptomycin, chlortetracycline, and sodium sulfadiazine were added

in full dosage. Whole blood was transfused. Diphenylhydantoin and phenobarbital sodium controlled the Jacksonian-type status epilepticus that developed. Right hemiplegia developed, and a tracheotomy was performed when Cheyne-Stokes respiration developed. When the patient became moribund, ristocetin was given intravenously in doses of 1 Gm. every six hours, along with 15 ml. of gamma globulin. Marked clinical improvement was evident on the second day of ristocetin therapy, and the patient went on to a recovery.

Experience with ristocetin in treating infections with gram-positive cocci was reported by Dascomb and West of Louisiana State University School of Medicine. Ristocetin was given to 11 cases with *Staphylococcus aureus* sepsis, pneumonia, or skin infection and to 1 case with urinary tract infection and bacteremia caused by a non-hemolytic *Streptococcus* and a *Pseudomonas* species. Total daily doses of 70 to 120 mg./Kg. given intermittently by vein provided satisfactory response in 7 cases. Similar doses in 2 cases revealed specific anti-coccal effect. In one the enterococcus promptly disappeared but chloramphenicol was required to eradicate the co-infecting *Pseudomonas*. The second patient with *S. aureus* infection of the skin improved initially but died abruptly with an *E. coli* superinfection. Treatment failed in 3 cases. Drug fever occurred in 7 patients. Three of these had associated skin rash and thrombophlebitis. The authors stated that total daily dose of ristocetin should be 4.5 to 6 Gm./day for adequate therapy of coccal infections in adults. Such doses result in frequent reactions.

Experiences with ristocetin in staphylococcal pneumonia were reported by Schumacher *et al.* of the U.S. Naval Hospital, St. Albans, New York. Twenty-three patients with staphylococcal pneumonia received ristocetin. In 7 cases it was the initial agent used. In the remaining 16, ristocetin was used following unsatisfactory response to multiple antimicrobial agents. There were two deaths directly attributable to pneumonia in the total series. The average daily dose was 25.6 mg./Kg. (ranging from 7.2 to 42.9 mg./Kg.). Six patients received a maintenance dosage exceeding 25 mg./Kg., 2 of whom developed moderate thrombopenia (60,000 to 80,000 cells/cu.mm.) with return to a normal range when the dosage was reduced to 25 mg./Kg. or less. The rapid clinical response achieved with these low blood levels reflects the adequacy of the dosage schedule. Ristocetin blood levels were obtained 8, 12, and 24 hours postdosage in 4 patients, and these levels ranged from 3 to 9 ug./100 ml. Toxicity was minimal.

The use of ristocetin in children and adults was discussed by Terry of the Northwestern University Medical School. Ristocetin was given to 23 patients with excellent results in 16. In the other 7 patients, only 2 received adequate therapy; one died from the primary cerebral hemorrhage, the other from an unsuspected suppurative arthritis. Case histories reveal that the response to ristocetin is somewhat delayed, usually until the third day, and fever disappeared only after four or five days. The pediatric experience was particularly gratifying and all 6 children responded well. Dosage ranged from 2 to 6 Gm. daily with a maximum total of 117 Gm. in 27 days. Initially ristocetin was given as a slow dilute intravenous infusion. Rate and concentration were gradually increased until one patient was successfully given 1 Gm. in 20 ml. of diluent in three minutes. This more rapid administration was judged to be more effective and it caused less venous thrombosis. No hematologic nor dermatologic toxicity occurred, and apart from one instance of fever, no significant ill effects were noted.

The use of ristocetin in the treatment of seven selected difficult cases was discussed by Miller and colleagues of the V.A. Hospital, Fort Howard, Md. Ristocetin has produced excellent results in eradicating, mitigating, or preventing infection in seven selected difficult cases. Five cases involved strains of *Staphylococcus aureus* which did not respond to chemotherapy with other antibiotics. Three of the 5 cases were severe chronic osteomyelitis and two were severe skin infections. One was multiple myeloma complicated by peritonitis which followed perforation of the colon and one was a case of chronic ulcerative colitis.

The influence of combinations of ristocetin and neomycin on intestinal aerobic microflora was discussed by Shidlovsky and Prigot of Harlem Hospital, New York. In a previous investigation, ristocetin reduced the aerobic gram-positive microflora in human stools by more than 90 percent. In the present study, undertaken to determine the influence of combined antibiotic medication on the aerobic bacterial population of the intestines, neomycin was added to ristocetin in two dosage schedules. One group of five patients received perorally 400 mg. of ristocetin and 4 Gm. of neomycin in four divided doses in one day. Four grams of each antibiotic was administered in one day, in divided dosage, to a second group of patients. The combination of the two antibiotics, each effective against different types of bacteria, was found to have a wide range of inhibitory activity on various fecal microorganisms. In cultures of stools taken 18 to 24 hours after termination of medication, the higher dosage of 4 Gm. of ristocetin plus 4 Gm. of neomycin produced the most consistent reduction in the number of colonies of the total aerobic bacteria, the gram-negative, the gram-positive and the staphylococcal flora. All groups of aerobic bacteria were reduced by more than 90 percent. The results on yeasts and fungi were inconsistent. The antibiotic combinations administered orally in this study were well-tolerated by all patients.

A comparison of the *in vitro* and *in vivo* activity of ristocetin, penicillin, and erythromycin was made by Holper *et al.* of Abbott Laboratories. The ratio of activity against streptococci was 131 for ristocetin, 2.8 for erythromycin, and 7.6 for penicillin. With pneumococci the ratios were 77 for ristocetin, 32 for penicillin, and 2.4 for erythromycin. A comparison of the ratios for each antibiotic shows clearly that in contrast to penicillin and erythromycin, ristocetin has a higher activity *in vivo* than expected from the *in vitro* activity of this antibiotic.

SPIRAMYCIN, an antibiotic from *Streptomyces amboFaciens*, was used in the treatment of various types of infections by David *et al.* of the University of Oregon Medical School and the Portland Public Health Clinic. Infections diagnosed and treated in the 62 hospitalized patients were: bronchopneumonia (9); pneumonitis (6); lobar pneumonia (1); wound, sinus tract, or suppurative lesions (19); furunculosis (7); pelvic inflammatory disease (3); pyelonephritis (10); and pyocystitis (7). Cultures of the sputum, urine, or pus in 50 patients showed 26 to harbor staphylococci, 11 with *E. coli*, 6 each with *Aerobacter aerogenes* or *Proteus*, and 7 in whom *Pseudomonas* was found. In the other cultures, in addition to some of these organisms, the usual streptococci, *Neisseria pharyngis* or *N. meningitis* or paracolon were found in sputum cultures and *Streptococcus faecalis* (1 patient) in the urine. Administration of spiramycin (available in 250 mg. tablets) was by four divided doses a day as follows: 1 Gm./day for 4 to 11 days to 7 patients; 2 Gm./day for 2½ to 17 days to 47 patients; 4 Gm./day for 4 to 20 days to 6 patients; and, in 2 patients, in increasing dosages from 4 to 6 Gm./day. The authors consider the response to spiramycin as "good" in 32 (51 percent) patients; "satisfactory," but not remarkable, in 22 (35 percent); "fair " in 7 (11 percent); and failure in 1 patient. No serious toxic effects were

noted. Mild side effects of loose stools, nausea, or pruritus ani were noted in 3 (16.6 percent) patients. The authors conclude that spiramycin in adequate dosage of 2 to 4 Gm. per day over a period of time compares favorably with novobiocin in its spectrum of activity.

The use of spiramycin for acute gonococcal urethritis in the male was reported by Marmell and Prigot of Harlem Hospital. The total dose used ranged from 2 to 8 Gm. of the drug. The dosage schedule employed was 500 mg. 4 times a day for from 1 to 4 days. Of the 16 patients treated on the 4 day schedule, 15 were considered cured. When 43 patients were given the drug for only 1 day, 33 were cured and 10 reported as failures. An allergic reaction, flushing and pruritic urticaria, was experienced by one patient who received a total of 6 Gm. of the drug. This individual, however, was also allergic to penicillin and tetracycline. In no other patient was there any toxic or allergic manifestation.

A 1 percent ophthalmic ointment or solution of spiramycin was used by Hurwitz of Chicago in 54 varied ophthalmic conditions, primarily in infectious external ocular conditions. The ointment was used in 41 patients and the solution in 13. Spiramycin in both forms was strikingly effective in improving or curing the various diseases. Results were better with the solution, for 2 patients developed irritative phenomena with the ointment, which was due probably to the vehicle and not to the drug. The solution was found clinically stable for 3 or 4 weeks. The author recommends the use of spiramycin in 1 percent ointment and 1 percent solution for local treatment of external ocular infectious conditions.

The ocular penetration and tolerance of spiramycin was tested in the eyes of albino rabbits by Furgiuele *et al.* of the Wills Eye Hospital in Philadelphia. Preparations used were solutions of spiramycin (0.5 to 5 percent) and ointments (1 to 5 percent). Tests were to determine tolerance and penetrability. The preparations mentioned were well-tolerated on normal eyes. The authors state that the high degree of sensitivity of *B. subtilis* to spiramycin suggests that it might be of value in the treatment of vitreous abscess due to this organism.

Studies by Benazet and Dubost of the Rhone Poulenc Company of Paris show that spiramycin attains high and persistent concentrations in the tissues. The authors draw attention to the insufficiency of *in vitro* activity tests and measurement of blood levels in judging the value of an antibiotic and state that the levels that occur in tissues should also be considered.

STREPTOVITACINS A and B have been isolated from the culture filtrate of a *Streptomyces* fermentation. Streptovitacins A and B are neutral, water-soluble compounds with the molecular formula $C_{15}H_{23}NO_5$. Both are stable in acid solution but degrade rapidly in alkali. The presence of an optically active chromophore was determined by rotary dispersion. Studies on the isolation and purification of Streptovitacins A and B were presented by Elbe *et al.* of the Upjohn Company.

Streptovitacin A is a new crystalline antitumor agent which was isolated following the work of Field *et al.* of the School of Medicine of the University of Southern California and the Los Angeles County General Hospital. In the course of their work, a fermentation product of a *Streptomyces* was obtained that gave in mice with Crocker sarcoma 180 a moderate but variable degree of tumor inhibition. This led to an evaluation of the remaining beer solids of the *Streptomyces* fermentation and resulted in finding that a suspension of the crude material given intraperitoneally produced a significant reduction of sarcoma 180 with an average reduction of the tumors to 51 percent of controls and was also effective when given orally.

Structure studies on streptovitacins A and B were reported by Herr of the Upjohn Company. Although aqueous titration of streptovitacin A indicated no titratable groups, the imide group was detected by nuclear magnetic resonance measurements. Treatment of streptovitacin A with strong acid gives a phenolic derivative which is identical with a product obtained from cycloheximide. These properties are most consistent with the structure 3-[2-(4-hydroxy-3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]-glutarimide for streptovitacin A. It is postulated that streptovitacin B is a stereoisomer of streptovitacin A.

Streptovitacin A has been evaluated under a variety of conditions in a spectrum of mouse and rat tumors by Field *et al.* of the School of Medicine, University of Southern California and the Los Angeles County General Hospital. The tumors studied included sarcoma 180, RC carcinoma, Ehrlich ascites, leukemia L 4946, and the Walker carcinosarcoma. A significant inhibition has been obtained against all tumors studied and in relatively minute quantities. With doses of approximately 0.5 mg./Kg. per day, the sarcoma 180 was inhibited to about 60 percent of controls by all routes utilized: intraperitoneal, intramuscular, subcutaneous, and oral. RC carcinoma was inhibited to 41 percent of controls by 0.6 mg./Kg./day of the new agent; with the same dose Ehrlich ascites tumor mice exhibited a prolongation of life of 56 percent beyond that of controls, and leukemia L 4946 tumors were reduced to 47 percent of controls with 0.5 mg./Kg./day of streptovitacin A, all intraperitoneal. The Walker carcinosarcoma of rats grew to about 50 percent of controls after 7 days when given 0.75 mg./Kg./day streptovitacin A intraperitoneal. When the new agent was given to mice with established 2, 3, or 4 day sarcoma 180 tumors, no significant inhibition was observed. Injection into tumors was also ineffective. Sarcoma 180, which was markedly inhibited by the new agent, when transplanted, grew irregularly. The tumors of treated animals showed marked disruption of normal growth with areas of liquefaction and necrosis. Extensive further studies are under way.

Biological studies on streptovitacin A were also carried out by Evans *et al.* of the Upjohn Company. The drug was tested against 2 mouse and 4 rat tumors. Five out of 6 of the tumors were inhibited when treatment was started within 24 hours after planting the tumors. Toxic symptoms noted at high dose levels were listlessness, diarrhea, and hematuria.

SULFADIMETHOXINE and SULFAMETHOXYPYRIDAZINE were the subject of four papers presented. A study on sulfadimethoxine was presented by Boger of the Norristown State Hospital, Pa. Sulfadimethoxine, 4-sulfanilamido-2 6-dimethoxypyrimidine, is a long-acting antibacterial sulfonamide. The drug is rapidly absorbed following oral administration and achieves high plasma concentrations within 4 to 6 hours. Levels above 10 mg./100 ml. are maintained for at least 24 hours following single oral doses of 2 Gm. The drug circulates largely in the form of free, antibacterially active compound, approximately 10 percent being in the conjugated form. About 6 percent of the administered dose is recovered in the urine within 8 hours. Fifteen to 25 percent of the drug recovered in the urine is in the conjugated form. Sulfadimethoxine diffuses promptly and moderately well through the uninflamed meninges into the cerebrospinal fluid. The drug has been compared in the same patients with sulfadimethoxine, sulfasoxazole, and sulfaethidole (sulfaethylthiadiazole). On the basis of the studies reported, this drug appears to offer

the potential of great flexibility of oral dosage schedules for all of the therapeutic and prophylactic uses of the sulfonamides.

Sulfadimethoxine was used in the treatment of 222 infants and children by Townsend and Borgstedt of The Rochester General Hospital. Plasma level studies indicated that plasma levels averaging about 14 mg./100 ml. were obtained 4 to 8 hours after a single oral dose of 30 mg./Kg. After 24 hours and 48 hours this had decreased to 9.5 and 5.5 mg./100 ml., respectively. Following the preliminary plasma level studies, the patients were routinely treated with an initial oral dose of 30 mg./Kg. of body weight followed by a single 15 mg./Kg. dose every 24 hours thereafter for 4 to 10 days. The disease categories treated were the more common pediatric conditions such as otitis media, bronchitis, respiratory and gastrointestinal infections. No side reactions were observed in the entire series of 222 patients. The authors conclude that the combination of antimicrobial effectiveness plus the lack of undesirable side effects make sulfadimethoxine an essentially useful drug.

TETRACYCLINES were discussed by several authors.

GLUCOSAMINE-POTENTIATED TETRACYCLINE in the prophylaxis and therapy of surgical infections was discussed by Mersheimer of Flower and Fifth Avenue Hospitals, New York. A clinical evaluation was performed in 55 successive cases of surgery in contaminated fields or of wound infections. In this series, the prophylactic and therapeutic results were excellent and no side effects were encountered in any patient.

Effectiveness of glucosamine-potentiated tetracycline in upper respiratory infections in children was discussed by Nathan of Skokie, Ill. The series included 100 febrile patients, primarily children, with upper respiratory infections and coincident complications. Bacteriological identifications were made in all cases. Microorganisms included alpha-, beta-, and non-hemolytic *Streptococcus*, gram-positive and gram-negative bacilli, *Micrococcus pyogenes, Neisseria catarrhalis* and *Diplococcus pneumoniae*. Glucosamine with tetracycline was found to be 77 percent effective in the treatment of these infections. Cures were generally observed within 2 to 3 days.

Kuck of the Research Division, American Cyanamid Company, studied the effect of triamcinolone, prednisolone, and hydrocortisone on the dose requirements of tetracycline for the control of a *Streptococcus* infection in mice and found that triamcinolone was more potent in its ability to increase the therapeutic dose requirements than were the other steroids mentioned.

POLYPHLORETINPHOSPHATE complexes of tetracycline and related compounds was the subject of a presentation by Bartner and Schaeffer of The Squibb Institute for Medical Research. Polyphloretinphosphate, a high molecular weight synthetic polymeric ester, is known to be a strong inhibitor of alkaline phosphatase and hyaluronidase. In an effort toward obtaining a method of prolonging the duration of parenterally administered tetracycline, complexes of polyphloretinphosphate and tetracycline were prepared. When aqueous solutions of tetracycline hydrochloride are reacted with dilute solutions of polyphloretinphosphate, yellow amorphous precipitates result which are complexes of the reactants. Their composition can vary over a wide range of weight ratios of the respective compounds. The stoichiometric equivalence point as determined turbidimetrically showed a ratio of approximately 1 part tetracycline to 1.1 part of polyphloretinphosphate. Similar reactions occur with chlor- and oxytetracycline. Solubility studies of the tetracycline complex in phosphate buffers at *p*H 2 to 7 showed that at a neutral *p*H, the complex possesses a considerably higher solubility than tetracycline base or other tetracycline compounds, while the reverse condition holds at an acid *p*H. Intramuscular injections of an aqueous suspension of tetracycline-polyphloretinphosphate complex gave rise to a lower incidence of tissue reaction in rabbits, and similar blood levels in dogs when compared to tetracycline phosphate complex. Preliminary studies on oral administration in dogs indicated an increasing and sustained blood level during the test period of 7 hours.

Results of sensitivity studies on CHLORTETRACYCLINE were reported by Weinstein and Welch of the Food and Drug Administration. The study was designed to test the sensitivity of persons with known allergy to therapeutic doses of chlortetracycline. The purpose of the study was to determine whether persons sensitive to therapeutic doses would react to very small doses. Seven patients were selected and the double blind method was used in administering capsules containing 0.5, 1.0, 5.0, and 25.0 mg. of chlortetracycline and also placebos containing lactose. Each patient received 8 capsules, four placebos and 4 doses of chlortetracycline, using a table of random numbers. Capsules were administered on successive days and the patient observed for at least 3 hours after administration to determine whether any reactions resulted. Six of the 7 patients showed absolutely no reaction to any of the capsules. One patient experienced a slight amount of itching two hours after the 1.0 mg. dose. This lasted approximately 15 to 20 minutes. There were no objective signs of a reaction. Furthermore there were no further reactions in this patient after the 5 and 25 mg. doses. It appears that sensitivity to the tetracyclines is rare and even when it does occur on therapeutic doses (250 mg.) it does not occur on doses up to 25 mg.

The effect of tetracyclines on enzymes was the subject of a presentation by Málek *et al.* of the Institute of Clinical and Experimental Surgery and the Biological Institute of the Czechoslovak Academy of Sciences. Antibiotics of the tetracycline group, especially chlortetracycline, decrease the activity of pancreatic enzymes alpha-amylase and lipase. This effect is more significant in the presence of some bivalent metal ions, such as calcium and magnesium and can be avoided by some organic acids, such as citric acid. By this activity of chlortetracycline on pancreatic enzymes, the resorption of some nutrients from the gastrointestinal tract is lowered so that not only resorption of chlortetracycline is diminished, but at the same time the excretion of pancreatic enzymes is lower. This is one of the causes responsible for the occurrence of side effects accompanying the oral use of antibiotics. The effect of citric acid on the enhanced concentration of antibiotics in the blood can, to a certain degree, be explained when the buffering activity of the tetracyclines on digestive enzymes is avoided. This antienzymatic effect of chlortetracycline can be successfully used for treatment of acute necrosis of the pancreas. The application of high doses of chlortetracycline decreases significantly the incidence of lipide necrosis. At the same time a greater survival rate of laboratory animals is achieved.

Price *et al.* of Chas Pfizer and Co. discussed the reversal of calcium inhibition of intestinal absorption of OXYTETRACYCLINE in chickens by certain acids and acid salts. Studies have indicated that serum levels of tetracycline-type antibiotics are diminished by exogenous calcium in the gut and that these levels are increased when the calcium complexing agents, sodium citrate and sodium metaphos-

phate, are added. In contrast, terephthalic acid, which is not known to form strong complexes with calcium, also has been shown to increase serum levels of these antibiotics. This study sought to determine whether these agents and certain others act by reversal of calcium inhibition of oxytetracycline absorption from the intestine. Oxytetracycline and test compounds were simultaneously injected into isolated, ligated intestinal loops of 8 to 10 week old chickens. Blood level enhancing effect was determined in the presence and absence of exogenous calcium supplied as calcium chloride with 2 molecules of water. Citric acid, sodium metaphosphate, potassium oxalate, and the tetrasodium salt of ethylenediaminetetraacetic acid were capable of bringing about partial to complete reversal of the depression in the oxytetracycline absorption caused by exogenous calcium. Kojic acid did not influence absorption of oxytetracycline in the presence or absence of exogenous calcium. Terephthalic acid increased oxytetracycline serum and liver levels in the presence or absence of exogenous calcium. Under both conditions, urine antibiotic concentrations were diminished by this agent.

The use of oxytetracycline in urinary tract infections was reported by Foret of the University of Leige, Belgium. The drug was evaluated in the treatment of acute and chronic urinary tract infections in 90 patients, including 6 cases of acute pyelonephritis, 23 cases of chronic pyelonephritis, 19 cases of acute cystitis, 25 cases of chronic cystitis, and 5 patients in whom the drug was used either preoperatively or postoperatively. Usually the patients received 1 Gm. of the drug daily in the form of capsules. All of the acute cases responded rapidly and 34 of the 48 patients having chronic infections responded satisfactorily.

Use of an insoluble oxytetracycline in the treatment of brucellosis was discussed by Lus of the University of Zaragoza, Spain. The principle of the method is based on the use of an insoluble preparation of the antibiotic, which, injected subcutaneously, would be phagocytized by polymorphonuclear leukocytes and monocytes and carried to the spleen and lymph glands where *Brucella* organisms are harbored. In this way, a higher antibiotic concentration becomes available at the site of active infection. Fifty-eight patients received treatment consisting of an initial injection of 80 mg. followed by 160 mg. each week for a total of 8 to 10 weeks. In 56 patients, therapeutic results were very satisfactory. The 2 remaining cases were resistant to antibiotic therapy.

The distribution and excretion of randomly labelled C^{14} oxytetracycline was reported by Leevy *et al.* of the Jersey City Medical Center and Seton Hall College of Medicine. In normal subjects a considerable amount of the drug is stored in the liver, as revealed by biopsy studies and initial difference in arterial and hepatic vein drug levels. Within one hour, large amounts of the antibiotic appeared in the bile. Less hepatic storage of oxytetracycline occurred in patients with cirrhosis and vascular shunts that bypassed the liver.

Helmer of the University of Vienna reported on the treatment of chronic pulmonary abscesses and pulmonary suppurations with oxytetracycline. Dosage used was 1 Gm. daily for at least 10 days, and in obstinate cases for one month. With oxytetracycline most patients were free of fever in two or three days except a few who became afebrile in 8 to 12 days. General health improved after one week; sputum quantity decreased within a few days. In contrast with good clinical and subjective improvement, objective improvement was very slow in 9 cases but the abscesses in these were two to three inches in diameter.

The topical use of antibiotics in the treatment of chronic skin ulcers was reported by Garre *et al.* of the University of Litoral, Rosario, Argentina. Oxytetracycline proved to be the most efficient of the therapeutic agents tested; sterilization time was considerably shorter than with the other solutions. Ulcers became sterile in the following percentage of cases and in the following average times: 93 percent of ulcers treated with oxytetracycline, in 56 hours; 72 percent with chloramphenicol, in 85 hours; 10 percent with tetracycline, in 114 hours; and 33 percent with erythromycin, in 160 hours.

In studying the prophylaxis of the common cold Ritchie of the Public Health Laboratory in Birkenhead, England found that the prophylactic administration of antibiotic troches suppressed and controlled nasopharyngeal organisms. Sensitivity tests showed the tetracyclines to be the most suitable for this purpose and his experience was largely with oxytetracycline troches. Of volunteers promptly reporting prodromal symptoms, only 4 out of 100 in the group receiving antibiotic prophylaxis developed all the manifestations of the complicated cold, as compared to 26 out of 100 of the controls. Of 1,120 volunteers in the winter of 1957-1958, only 6.2 per 100 of those on antibiotic prophylaxis developed significant symptoms, while 22.7 per 100 of the control group developed severe nasopharyngitis.

PROPHYLAXIS OF OPHTHALMIA NEONATORUM was the subject of a presentation by Posner *et al.* of Harlem Hospital who had studied the effects of various antibiotics for the protection of the eyes of the newborn. When results of these studies were compared to the results obtained with the use of silver nitrate, it was concluded that despite the chemical irritation of the eyes of the newborn which silver nitrate occasionally produces, silver nitrate instillation remains the most effective and safe method of prophylaxis of ophthalmia neonatorum.

TRIACETYLOLEANDOMYCIN and its biochemical correlations was the subject of a presentation by Celmar of Chas. Pfizer and Co. Triacetyloleandomycin, $C_{41}H_{67}NO_{18}$, is a biochemically active, completely acetylated chemical variant of oleandomycin. The acetyl substituents in triacetyloleandomycin reside in three distinct structural moieties, namely, the sugars desosamine (R_1) and levo-oleandrose (R_2) and the macrolide nucleus oleandolide (R_3). Homologous triesters and all of the theoretically possible mono- and diacetate esters were employed as model compounds in further studies on triacetyloleandomycin. Pertinent properties of triacetyloleandomycin such as stability, solubility in lipid solvents, *in vitro* potency, and *in vivo* activity were correlated with particular acylation sites and acyl species. Novel *in vivo* deacetylation sequences were observed in connection with investigations on the metabolism of triacetyloleandomycin and related esters in human subjects. A variety of metabolic pathways followed by triacetyloleandomycin accounts for the multiple microbiologically active components observed and identified in blood serum and urine specimens.

Triacetyloleandomycin was used clinically in a wide variety of cases by Karelitz and Isenberg of the Long Island Jewish Hospital. Triacetyloleandomycin, given orally 40 mg./Kg./day in children and 2 Gm. daily in adults, was tested in a group of 53 patients and contacts suffering from a variety of pyogenic infections predominantly due to *Staphylococcus aureus*. The results were good in 45, fair in 3, and 5 were not helped. Of 11 cases of pneumonia, 2 due to *D. pneumoniae* and 9 to *Staphylococcus aureus*, 10 responded rapidly and one slowly. Tonsillitis caused by group A beta hemolytic streptococci responded promptly.

Two of 3 children hospitalized with pyogenic skin infection had good results, 1 poor; 5 children with recurrent furunculosis and 8 of their contacts were successfully treated. Seven carriers of *Staphylococcus aureus,* type 80/81 among nurses and doctors probably responsible for a nursery epidemic of conjunctivitis, pyoderma, and omphalitis due to this strain, responded to 4 days of treatment, 2 Gm. daily. Purulent otitis media (2), postoperative peritoneal abscess (1), cervical adenitis (2), and tonsillitis and pharyngitis (4) responded to therapy. One of the upper respiratory infections, probably viral, failed to respond but *D. pneumoniae* present in the pharynx disappeared with treatment. Six of the 53 treated individuals acquired resistant bacteria. A sensitive VA 4 strain of *Staphylococcus aureus* recovered from the infant with pulmonary fibrosis became resistant to oleandomycin after 7 days of therapy. *H. influenzae,* oleandomycin-resistant, was recovered from a 3 year old diabetic girl with tonsillitis, who had had *Staphylococcus aureus* and *D. pneumoniae* in the throat before. The other oleandomycin treated bacteria were nonpathogenic commensals such as *Str. viridans.* Two of the failures were in children with cystic fibrosis and chronic pulmonary disease, 1 in an infant with pulmonary hypertension and congenital heart disease, 1 leukemia with multiple furuncles, and 1 with a viral upper respiratory infection. Complications of therapy included: one child vomited repeatedly after 24 hours of therapy, one child developed diarrhea after 5 days of therapy, one child developed hepatitis after 3 weeks of treatment from 1 to 2 Gm. daily. This probably was viral hepatitis. The others took the drug well and had no ill effect.

The treatment of lymphogranuloma venereum with triacetyloleandomycin was reported by Loughlin, Alcindor, and Mullin. Twenty-seven patients, all Frei positive, were treated. A dosage of 1 Gm. of the drug was given twice daily for 5 days. Regression of a lymphadenitis generally was rapid, and was apparent by the fourth or fifth day. However, in 11 cases, where regression of the lymphadenitis seemed slower, the above dosage was repeated after one week. None of the patients—all of whom were observed for periods of three to eight months post-treatment—have relapsed. There were no toxic reactions. The authors believe that triacetyloleandomycin is a superior antibiotic in the treatment of early lymphogranuloma venereum.

The use of triacetyloleandomycin in pediatric infections was reported by Mellman *et al.* of the Hospital of the University of Pennsylvania. Forty patients were given the drug in oral suspension in doses of 10 mg./lb./dose every six hours. Eighty-five percent of the febrile diseases showed remission in less than 48 hours. In 30 instances a predominating bacteriological diagnosis was made. Twelve out of 15 responded favorably when *Staphylococcus aureus* was the predominating organism; 4 out of 4 with pneumococcus; 5 out of 5 with *Streptococcus;* 5 other cases with predominantly gram-negative organisms were also treated with less satisfactory results. The drug was given for as long as 31 days without serious toxicity. In 3 patients the drug was discontinued because of rash or vomiting.

The use of triacetyloleandomycin in the treatment of acne and pyodermas caused by resistant *Staphylococcus aureus* was reported by Olansky and McCormick of Duke University Medical Center. Forty patients with pustular acne and 21 patients with infections caused by *Staphylococcus aureus* that was resistant to one or more other antibiotics were treated.

Kaplan and Goldin, of the Allergy Research Unit and Mount Sinai Medical Research Foundation in Chicago, reported on the use of triacetyloleandomycin in chronic infectious asthma. Forty patients were placed on 250 mg. of the drug three times a day. The main effect noted after from five days to three months treatment was a marked diminution in the amount of sputum in approximately 50 percent of the patients. Cases that previously required frequent therapeutic bronchoscopies no longer needed this treatment. There were no extreme alterations in the bacterial flora of the sputum. No strains of gram-positive cocci that had developed resistance to the drug were encountered.

Loughlin *et al.* reported results of a study of the comparative efficacy of triacetyloleandomycin, erythromycin, and penicillin V in the treatment of acute gonococcal urethritis. Three hundred and forty-one cases were treated, all males. Two hundred and six patients were treated with triacetyloleandomycin administered in a single oral dose of 1 Gm.; 70 patients were treated with erythromycin stearate, administered in a single oral dose of 1 Gm.; and 65 patients were treated with penicillin V potassium (phenoxymethyl penicillin) administered in three oral doses of 600,000 units each at intervals of six hours. Triacetyloleandomycin cured approximately 94 percent of the patients; erythromycin stearate approximately 86 percent; and phenoxymethyl penicillin approximately 84 percent.

TRIAMCINOLONE used as an adjuvant in the treatment of tuberculosis was discussed by Pilheu and colleagues of Hospital Muniz, Buenos Aires, Argentina. The authors find that triamcinolone is a useful adjuvant in the treatment of certain forms of tuberculosis. The following conditions are essential when employing this hormone: that the germs be sensitive to the drugs used (streptomycin, PAS, isoniazid, etc.); that isoniazid be included in the treatment; and that blood glucose be at a normal level. The best results achieved are with very severe tuberculosis (including meningitis), tuberculosis associated with another disease where an improvement is possible through corticotherapy (asthma and arthritis), and hypersensitive to some anti-tuberculous medication.

VANCOMYCIN is an antibiotic obtained from a species of *Streptomyces orientalis.* Clinical evaluation of vancomycin in multi-antibiotic refractory staphylococcal infections was undertaken by Ehrenkranz of the University of Miami School of Medicine. Ten patients with active staphylococcal infections were critically ill with pneumonia, bacteremia, arthritis, osteomyelitis, meningitis, and massive parotitis in spite of previous treatment with two to five other antibiotics for five days to six weeks. Vancomycin dosage was 1.5 to 2.0 Gm./day, intravenously, for 7 to 16 days. Results of treatment were successful in 7 patients and this was considered a good result considering the infection appeared to be life-threatening in 9 cases. Four persons were cured by vancomycin alone, 3 were sufficiently improved that their subsequent surgical drainage was possible, and 3 died of their infection. Side effects were limited to thrombophlebitis in 1 patient, fever in 1, and rash in 3.

The present status of vancomycin in therapy of staphylococcal and streptococcal infections was reported by Kirby *et al.* of the University of Washington School of Medicine. Thirty patients with severe staphylococcal and streptococcal infections were treated with vancomycin during the past year. Sixteen had positive blood cultures. Results were, in general, excellent and were often dramatic in instances where other antibiotics failed. The authors state that vancomycin is probably the best drug now available for the treatment of severe staphylococcal infections. They state that the clinical material now available is much better tolerated and produces relatively few side effects.

A S H P

EXECUTIVE COMMITTEE ACTIONS

October 1958 Meeting

► THE EXECUTIVE COMMITTEE of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS met at the Marott Hotel in Indianapolis, Indiana on October 23, 24, 25 and 26. Members of the Committee attending included: Robert C. Bogash, Clifton J. Latiolais, Gloria N. Francke, Sister Mary Berenice, Allen V. R. Beck, Louis Jeffrey, Robert Lantos, Jack McNamara, and Leo F. Godley. One member of the Executive Committee, Dr. William Heller, was unable to be present. Vernon O. Trygstad, Vice-President Elect, participated as a member of the Committee in the absence of Dr. Heller, President-Elect. Others participating in various parts of the meeting included: Dr. Robert P. Fischelis, Secretary of the American Pharmaceutical Association; Dr. William Apple, Assistant Secretary of the American Pharmaceutical Association; Paul F. Parker, Director of the Division of Hospital Pharmacy of the A.Ph.A. and the ASHP; Joseph Oddis, Staff Representative of the Council on Professional Practice of the American Hospital Association; and Don E. Francke, Editor of the *American Journal of Hospital Pharmacy*. George F. Archambault and Grover C. Bowles, who were invited in connection with special activities, particularly the American Hospital Formulary Service, were also present for the Saturday meeting. Sister Mary David, companion to Sister Mary Berenice, also attended.

The group met for three days beginning on Thursday evening and continuing through Friday, Saturday and Sunday. Thursday evening was devoted to consideration of the reports of special committees by individuals assigned to study them and report back to the Executive Committee with specific recommendations for action. As will be noted from the summary of actions taken by the Executive Committee, numerous important items came before this group for consideration.

In order that SOCIETY members will be informed concerning Executive Committee actions, those of particular note are outlined in the following paragraphs.

Membership and Affiliated Chapters

After consideration of detailed report on membership activities and the status of affiliated chapters, the Executive Committee took the following actions:

—Voted to take the matter of membership in affiliated chapters with regard to individual membership in the A.Ph.A. and the ASHP, under advisement, and refer to the Committee on Constitution and By-Laws.

—Agreed that it is advantageous to receive the two billings for A.Ph.A. and ASHP membership in one mailing (as either a joint statement or two separate bills).

—Approved affiliation of the Arkansas Association of Hospital Pharmacists calling attention to the Secretary's letter stating that if the members do not join the A.Ph.A. and the ASHP, they "will not be considered members of the (Arkansas) Association."

—Approved the Southern Appalachian Society of Hospital Pharmacists as an affiliate of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, directed the Secretary to point out that members who are not affiliated with the A.Ph.A. and the ASHP must either join the National organizations or be dropped from the local group.

—Voted to call attention of the affiliated chapters to the fact that any changes in Constitution and By-Laws of the local groups should be forwarded to the Secretary and called to the attention of the Executive Committee.

Minimum Standards

Particular attention was given to the proposed plan for revision of the Minimum Standard for Pharmacies in Hospitals and the following action taken:

—Voted that, in order to appeal to all the ASHP members for assistance in the proposed revision for the Minimum Standard for Pharmacies in Hospitals, an open letter be published in the AMERICAN JOURNAL OF HOSPITAL PHARMACY.

In accordance with this action, a letter directed to the members and affiliated chapters from the Chairman of the Committee on Minimum Standards was published in the November issue of the JOURNAL. Included with the letter was a copy of the Minimum Standard and the Guide to Application of the Standard.

Program and Public Relations

Attention was given to the work of the Committee on Program and Public Relations and subjects and speakers for the Annual Meeting and the 1959 Insti-

tutes were considered. In developing plans for the 1959 Annual Meeting, consideration was given to the program, Business Session, House of Delegates' Meeting, the H.A.K. Whitney Award Dinner, and Special Events.

Pharmacists in Government Services

On presenting the areas of interest in connection with the work of the Committee on Pharmacists in Government Services, it was noted that the Committee's activity has not been clarified. In view of this, the Committee Chairman was asked to evaluate the work of the Committee, its purpose and name, and report to the Executive Committee for discussion and referral of recommendations to the Committee on Constitution and By-Laws.

American Hospital Formulary Service

Careful consideration was given to all phases concerned with the production, distribution and promotion of the American Hospital Formulary Service. Detailed reports were received from the Chairman of the Committee on Pharmacy and Pharmaceuticals with regard to the status of monographs and the Secretary reported on promotion and distribution. In summary, the following actions relating to the American Hospital Formulary Service were taken by the Executive Committee:

—Considered in detail plans for promoting and distributing the American Hospital Formulary Service, and

—Voted that a brochure on the Formulary Service and the development of the formulary system in hospitals be written and published prior to the next Annual Meeting if practical, and

—Voted that the Division of Hospital Pharmacy should be requested to further promote the Formulary Service as part of the exhibit at the Annual Convention of the American Hospital Association and the Catholic Hospital Association as in 1958, and

—Voted that the printer be directed to proceed graphs (with the exception of certain sections which graphs (with the exception of certain sections which were later added).

—Authorized the Chairman of the Committee on Pharmacy and Pharmaceuticals to proceed with establishing a class of manufacturers' consultants to provide significant pharmaceutical, pharmacological and clinical data on drugs, and drug products being considered for the Formulary Service, and further, that contacts be made with selected pharmaceutical firms in accordance with whatever methods seem most satisfactory.

—Approved appointment of Mr. Clifton J. Latiolais to the Committee on Pharmacy and Pharmaceuticals.

—Authorized the Director of the Formulary Service to appoint a second assistant to help in the preparation of initial monographs for the Formulary Service.

—Ask that, to the extent possible and depending on timing, all monographs in final form be submitted for review and final approval by members of the Reference Committee.

—Approved complimentary subscriptions of the American Hospital Formulary Service to specific individuals and institutions who have contributed in an outstanding way to the Formulary Service.

—Agreed that since bulk compounding formulas can logically be developed through the Committee on Pharmacy and Pharmaceuticals and related to the Formulary Service, the Executive Committee suggests that the Chairman of the Committee on Compendium on Bulk Compounding Formulas recommend in his annual report that the Committee be discontinued and further action be suspended until such can be studied by the Committee on Pharmacy and Pharmaceuticals.

—Considered in detail the legal implications with regard to the Formulary Service and the wording of the Preface and other statements to be included along with the monographs.

Relationships with Industry

The Executive Committee gave careful consideration to the alleged substitution problem in hospitals, recent developments in this area, and the role of the National Pharmaceutical Council. Following a detailed discussion and a number of constructive suggestions, the Executive Committee

—Voted to continue the Liaison Committee which would be kept "on call' in connection with actions taken by industrial groups. Further, the Committee would consider developing a long range plan for keeping the ASHP membership informed.

As a point of information, this Committee includes: Leo F. Godley, *Chairman,* Harris Hospital, Fort Worth, Tex.; Don E. Francke, University Hospital, Ann Arbor, Mich.; Grover C. Bowles, Baptist Memorial Hospital, Memphis, Tenn.; Walter M. Frazier, Springfield City Hospital, Springfield, Ohio; Paul F. Parker, Division of Hospital Pharmacy of the A.Ph.A. and the ASHP, Washington, D.C.; Sister Mary Berenice, St. Mary's Hospital, St. Louis, Mo.; Vernon O. Trygstad, Veterans Administration, Washington, D.C.; and Gloria Francke, Secretary ASHP, Ann Arbor, Mich.

It was further agreed that the affiliated chapters should be kept well informed concerning recent developments in this area and they should understand the SOCIETY's stand on the alleged substitution problem.

American Journal of Hospital Pharmacy

In considering the publications' program of the SOCIETY and the report of the Committee on Publications, it was

—Voted that the Committee on Publications shall be a Standing Committee of and shall report directly to, the Executive Committee. It was further

—Voted that the Committee on Publications shall consist of three members of the Executive Committee.

With regard to the functions of the Committee, the Executive Committee

—Voted that the functions of the Committee on Publications shall be to advise the Editor and inform the Executive Committee on the conduct of operations of the SOCIETY's publication and to suggest policy as it relates to the qualitative and quantitative aspects of editorial and advertising content of this publication. It was further

—Voted to review the financial operation of the SOCIETY's publication and to make recommendations for changes in policy and accounting procedures if such are indicated.

Research and Development

On considering the status of the SOCIETY's program on Research and Development, it was pointed out that two areas in which problems exist include (1) clarification of the SOCIETY's tax status and (2) the committee procedures for carrying out the activity. Accordingly, it was

—Voted that the Secretary be requested to investigate and clarify the tax exempt status of the SOCIETY with regard to accepting and disbursing research funds prior to the 1959 ASHP Annual Meeting.

With regard to the Committee report and the status of the current committee, it was

—Voted that the Executive Committee discontinue the present Committee on Research and Development (since the purpose of the committee cannot be achieved) until the tax status situation is clarified.

In clarifying the interim handling of the committee activity, it was agreed that the Selection Board would continue and the existing procedures would be handled with Paul Parker, Director of the Division, continuing to serve as Secretary. This means that requests for grants would be directed to Mr. Parker and contacts with the Selection Board would be made through him.

In planning for the future of this activity, it was

—Voted that upon clarification of the tax status, the Executive Committee establish some mechanism for developing general policies for awarding grants and complete administrative procedures for administering grant funds.

Establishment of a Whitney-Spease Scholarship Fund

In accordance with the recommendation from a special committee appointed to consider methods for recognition of Mr. H. A. K. Whitney and Dean Edward Spease, the Executive Committee

—Voted that the SOCIETY establish a fund to be known as the "Whitney-Spease Award Fund of the ASHP" and that a contribution of fifty dollars from the SOCIETY be made in order to initiate the fund. It was further suggested that details for carrying the plan out be referred to the original committee. (Walter M. Frazier, *Chairman;* Alex Berman; I. Thomas Reamer; and Evlyn Gray Scott). It was emphasized that this was to be a *voluntary* contribution and that attempt should be made to notify the affiliated chapters and members through the JOURNAL and possibly by direct letters to individuals who would be interested.

Miscellaneous

The Executive Committee's attention had been called to a proposal for a training program for pharmacy technicians. After discussing the problems which such a program might create with regard to use of nonprofessional personnel, the following action was taken:

Whereas it has come to the attention of the Executive Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS that a proposal to institute short courses for pharmacy technicians is being actively considered by certain hospital organizations, and

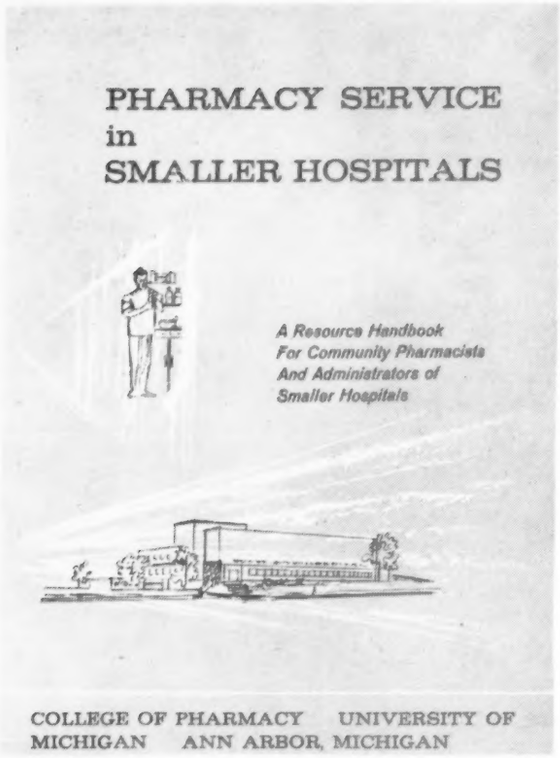
Whereas such a proposal may undermine the present educational program of our profession and mislead young people seeking a career in the health field, especially in pharmacy, and

Whereas these proposed short courses endanger public health by not providing competent professional training for adequate safety of patients,

Be It Resolved that the Executive Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS express its concern over this reported development and alert the local chapters of the ASHP to the dangers of any proposal that seeks to create a substandard program of pharmaceutical education which can only lead to a lowered standard of pharmaceutical service, and

Be It Further Resolved that the American Council on Pharmaceutical Education, the American Pharmaceutical Association, the American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy be requested to investigate these proposals immediately and take such action as may be indicated.

In addition to the significant actions reported above, the Executive Committee received numerous reports from the chairmen of the special committees, the officers, the Director of the Division of Hospital Pharmacy, the Chairman of the Policy Committee of the Division of Hospital Pharmacy and from representatives from the American Hospital Association and the Catholic Hospital Association.



PHARMACY SERVICE IN SMALLER HOSPITALS

► PHARMACY SERVICE IN SMALLER HOSPITALS is the title of a resource handbook for community pharmacists and administrators of smaller hospitals. This work has been compiled and is edited by Dr. Alex Berman who is Assistant Professor of Pharmacy in the College of Pharmacy at the University of Michigan and Mr. John J. Zugich, the Assistant Director of The University of Michigan Medical Center in Ann Arbor. Publication of the Handbook is the result of the need shown by a statewide study of the service potential of community pharmacists to hospitals, conducted by the University of Michigan College of Pharmacy during 1956-1957. The study was supported by a grant made to the College of Pharmacy by the University of Michigan from funds appropriated by the State Legislature for research in the utilization of human resources.

The Handbook, which measures approximately 8" x 10" in size, is divided into five main sections.

The Introduction states the objective of the work which is to assist the community pharmacist and the administrator of a small hospital by providing basic information on the philosophies and methods of drug distribution in hospitals.

Section II is entitled "Meeting the Hospital Administrator for the First Time." Its seven pages are devoted to What the Retail Pharmacist Should Know, Who Organized and Owns the Hospital, Who Directs the Hospital, What the Hospital Aims to Do, The Hospital Family, Departments, Combined Services, The Place of Pharmacy, The Administrator, The Administrator's Problems and Attitudes, and How Drug Orders Come to You in the Hospital.

Section III enumerates the "Principles of Affiliation." This section contains an 18 page discussion of the Philosophy of Service, Responsibilities and Functions, Facilities, Policies, Organization, Personnel, Pharmacy and Therapeutics Committee and the Hospital Formulary System, and Automatic Stop-Orders on Potent Drugs.

"Procedural Guides" is the subject of Section IV. This 27 page section contains guides to Purchasing, the Hospital Formulary, Drug Charges, Records, Basic Drug Stocks for Nursing Units, Safety Factors, Storage, and Staff Education.

Section V, the "Resource References," is the largest section of the Handbook and contains 169 pages. There are 14 subsections, each of which contains either complete articles or summaries of articles taken from the literature.

The authors have done an excellent work in compiling this Resource Handbook on Pharmacy Service in Smaller Hospitals. It should prove invaluable to the community pharmacist who wishes to give pharmacy service to the smaller hospital. It will also provide valuable guidelines to the administrator who wishes to bring such service to his hospital. In their preliminary discussions, both the community pharmacist and the administrator will find Section III, "Principles of Affiliation," of particular value in helping them reach an understanding of the responsibilities of each. Particularly significant are the policies which are quoted beginning on page 23. Here it is emphasized strongly that the community pharmacist is expected to give a personal, professional service within the hospital, as well as to sell drugs to the hospital and fill prescriptions for hospitalized patients.

This 263-page Handbook will also prove of great interest to practicing hospital pharmacists and should prove valuable to students taking orientation courses in hospital pharmacy. It is available from the College of Pharmacy of the University of Michigan in Ann Arbor and the cost is $3.00 per copy.

Therapeutic Trends

edited by WILLIAM JOHNSON

Desertomycin

Desertomycin, a new antibiotic of the streptomyces strain, is named after its source, African desert sand. Desertomycin is a uniform snow-white, glittering, crystalline, product and its tentative empirical formula is: $C_{33}H_{60\text{-}62}O_{14}N$. It melts at 189-190°C; is not very soluble in water, absolute alcohols, ether, or acetone. It is fairly soluble in alcohols which contain some water and its neutral aqueous solution is very stable. The substance gives acetylated and hydrogenated derivatives; it decolorizes a solution of permanganate or bromine; and gives positive ninhydrin and Kuhn-Roth C-methyl tests. Crystalline desertomycin was tested against a number of bacteria by serial dilution method (the minimum inhibitory concentration varies between 5 and 25 ugm/ml.), and it exhibits a very significant cytotoxic effect. In experiments it shows that it inhibits the life-activity of leukemic cells and of Ehrlich ascites cells. It exhibits a cytostatic action in low concentration but in higher concentrations a cytolytic action on fibroblast, HeLa and Crocker cells as studied by the tissue culture method. Once more the inhibition of the growth of bacteria is seen to be connected with the inhibition of tumor cells. This report appeared in *Nature 182*:401 (Aug.) 1958.

W. E. HERSHBERGER

Dimethoxanate

Dimethoxanate has been evaluated in more than 65 patients who required an antitussive agent. In 15 patients with severe chronic cough, dimethoxanate was thoroughly evaluated over a six-month period. Excellent to good results were obtained in 14 patients. No toxicity or side effects were noted. A long term study would be necessary to substantiate completely the absence of toxicity and/or persistance of efficacy. The small number of patients in the test group is partly compensated for by their selection (severe chronic coughers) and the thorough knowledge of their reliability and personalities because of prior study. The important subjective factor in evaluation of a symptom, such as cough and the personal equation in the response to a drug, removes an appraisal from a strict scientific basis. A placebo control was used to minimize personal factors. A comparable efficacy and acceptability were found in 50 other patients for whom dimethoxanate was prescribed as the routine antitussive. The study indicates that dimethoxanate is, in modern terminology, a "cough tranquilizer" in that the cough reflex is calmed but not abolished. Thus its action does not interfere with the useful function of the cough. Dimethoxanate is produced by the Ayerst Laboratories under the trade name of Cothera. The above report appeared in *Antibiot. Med. Clin. Ther. 5*:462 (July) 1958.

W. E. HERSHBERGER

Actinomycin—D

The antibiotic actinomycin D, is one of a group of closely related actinomycins. Actinomycin D produced a range of nonspecific cytotoxic changes in human neoplastic and normal primary tissue cultures. Neoplastic primary cultures were generally more sensitive to the action of actinomycin D than normal primary cultures, as judged by their cytological changes. On the other hand, both showed marked reduction in mitosis. Both neoplastic and normal established cell strains showed only mild sensitivity to the same concentrations of actinomycin D that damaged primary cultures. Sensitivity was indicated by an increase in the number of aberrant metaphases. There were relatively fewer aberrant metaphases in treated HeLa cultures as compared with conjunctiva and kidney cultures. A selective response to actinomycin D has been shown to exist among the primary cultures included in this study. In view of these observations, further study of the use of primary cultures for evaluating the *in vitro* effects of a potential chemotherapeutic agent is suggested. Actinomycin D used in this investigation as reported in *J. Nat. Cancer Inst. 21*:263 (Aug.) 1958, was furnished through the courtesy of the Lederle Laboratories.

W. E. HERSHBERGER

THQ For Keloids

Conclusions reached from four years of experience with tetrahydroxyquinone (THQ) as an oral treatment for keloids suggest that keloids of all ages show some response to this drug. There are definite changes in all the elements of the dermis and the more complete regression is obtained in younger keloids. Further, THQ is selective in its action and its effect may be mediated by enzymatic action. Kelly and Pinkus, in *A.M.A. Arch. Dermatol. 78*:348 (Sept.) 1958, report that in 45 cases treated there was first a lessening of tension and of pain and pruritus, so often associated with keloids. Young lesions tended

to respond more rapidly and the keloids became softer to palpation. Dosages varied from 30-180 mg. daily. No side effects or untoward reactions were observed as previously demonstrated by comparatively tremendous doses given to animals. The disadvantages of THQ treatment are that it is tedious and slow in action and is ineffective in treating large keloids. Tetrahydroxyquinone was supplied in part by Receiving Hospital Research Corporation and in part by a grant from the Paul Elder Co., Bryan, Ohio.

SYLVIA SCHMIDT

Sulfur Dioxide—Diagnostic Aid In Pulmonary Cancer

Since valuable information can be obtained from the sputum of individuals with suspected cancer, a survey was made of agents that would produce cough and bronchial secretions rapidly, transiently, and without serious or distressing extra pulmonary effects. Sulfur dioxide was selected for trial as potentially the most suitable of these agents. A control group of nine healthy young adults received a placebo, isoproterenol hydrochloride, and sulfur dioxide by nebulizer. Sulfur dioxide was so packaged that each valve released 0.24 mg. of the chemical. Three to six inhalations were given with each agent over a 10-minute period. Sulfur dioxide administration was followed by sputum production in from 5-45 minutes in all nine subjects while only three responded to isoproterenol HCl. These same three agents were then used in 25 possible pulmonary cancer cases at Johns Hopkins Hospital. All 25 produced sputum after SO_2 inhalation, 17 after isoproterenol hydrochloride, and 10 after the placebo. Nineteen exhibited no malignant cells in the induced sputum and further procedures failed to demonstrate pulmonary cancer. Five of six patients who did exhibit cells responded so after sulfur dioxide administration. There was a confirmation of pulmonary cancer through tissue section exams of all six patients. Continuation of these studies is still in progress as related by Allen Whittlesey, and Haroutunian with technical assistance of Elizabeth Relley in *Cancer 11*:938 (Sept.-Oct.) 1958. The materials were supplied by Riker Labs. Inc., Los Angeles, Calif. in the Riker Medihaler.

SYLVIA SCHMIDT

Virac—Iodophore

According to a report in *Arch. Ophth. 60*:206 (Aug.) 1958 by Harris *et al,* research to study an iodophore (Virac) was conducted at the John Weeks Memorial Laboratory and Clinics, Department of Ophthalmology, University of Oregon Medical School. Virac proved to be less toxic than benzalkonium chloride both *in vitro* and *in vivo*. Of all diluents used, boric acid was found to be the best from the stand point of compatibility and stability of the iodine. Even with this diluent, loss of elemental iodine occurs over a period of weeks under ideal conditions and more rapidly when the preparation is in contact with some contaminant such as metal or organic matter. In dilutions with considerable germicidal potency, Virac was not toxic to the human eye when applied to an eye with disturbed corneal epithelium. Virac appears to be an efficient surgical preparation. Its use around the eye prior to surgery caused no untoward local or other reactions. Virac appears to be an excellent irrigant for the conjunctival sac and lacrimal passages, being of low toxicity while possessing high germicidal activity. Virac is not a cure-all for ocular infections. It does not cure herpes simplex of the cornea but may be of value in its treatment. It is compatible with fluorescein, pilocarpine nitrate, methylcellulose, and scopolamine hydrobromide but not with atropine sulfate and carboxymethylcellulose. Virac has the advantage of providing an iodine preparation which does not stain the skin, has low iodine vapor pressure, and is not caustic. Further study as to the effectiveness as a surgical scrub is being conducted.

W. E. HERSHBERGER

Soframycin—New Intestinal Bactericide

A new antibiotic, framycetin sulfate, isolated from *Streptomyces lavendulae,* has been studied for use in intestinal surgery. The drug as described by Convell and Rousselot in *Surgery 44*:447 (Sept.) 1958, is minimally absorbed following oral therapy and is nontoxic. No untoward effects on the hematopoietic, hepatic, renal, cardiovascular or nervous systems were found in this study of 45 patients. Rapid fecal suppression occurred in the nonobstructed colon in comparatively low dosages. At least three grams of framycetin sulfate (Soframycin) per day for 48 hours is optimal for adequate control. This dosage regimen is in contrast to that for neomycin, which is at least double. No supplemental drug therapy such as nystatin or an insoluble sulfonamide in combination with framycetin for broader coverage seems indicated or necessary. There were few instances of predominance of yeasts concomitant with its period of activity and high bactericidal effect. The mucosal tissues obtained at surgery and postoperative studies indicate a high suppressive power of 36 hours after cessation of oral therapy. Soframycin's merits, therefore, consist of a palatable low-dosage antibiotic that is singularly nontoxic with a wide spectrum of bacterial activity and with rapid suppressive activity during a 2-day bowel preparation. Further studies are in progress to see if better control can be secured in obstructive lesions of the colon and in diarrhea. Soframycin was supplied by Roussel Corporation, New York City, N.Y.

SYLVIA SCHMIDT

Timely Drugs

Bradosol Lozenges

CHEMICAL NAME: A synthetic quaternary ammonium compound; dodecyldimethyl (2-phenoxyethyl) ammonium bromide.

INDICATIONS: For relief of pain and for active treatment of sore mouth, sore throat, tonsillitis, and other oral infections due to susceptible bacteria and fungi; may also be used prophylactically following dental or other surgical procedures of the mouth and throat.

DOSAGE: One lozenge, dissolved slowly, in the mouth as needed.

PREPARATIONS: Lozenge contain 1.5 mg. Bradosol, together with 2.5 mg. benzocaine.

PACKAGING: Package of 24 lozenges.

SUPPLIER: Ciba Pharmaceutical Products.

Celginace

COMPOSITION: Dioctyl sodium sulfosuccinate and the calcium and sodium salts of alginic acid.

INDICATIONS: Constipation characterized by difficult or infrequent defecation due to inadequate fecal volume, with low residue diets, with the ingestion of such substances as barium which tend to cause hard stools, when defecation is painful as in post partum or after surgical procedures involving pelvic and perineal areas.

SIDE EFFECTS AND CONTRAINDICATIONS: Should be used with care when symptoms suggesting partial intestinal obstruction, diverticulitis or diverticulosis, or appendicitis are present.

DOSAGE: Adults, 1 tablet or heaping teaspoonful 1 to 3 times daily with glass of water or juice; children, proportionately lower dosage based on age and weight.

PREPARATIONS: Tablets and granules.

PACKAGING: Bottles of 30 and 60 tablets, and cans of 147 Gm. (5 oz.) and 294 Gm. (10 oz.) of granules.

SUPPLIER: Mead Johnson.

Compocillin-VK

GENERIC NAME: Potassium penicillin V; potassium phenoxymethyl penicillin.

INDICATIONS: For all infections amenable to oral penicillin therapy; as a prophylactic agent against recurrence of rheumatic fever, in the management of rheumatic carditis, and in preventing secondary bacterial infection.

SIDE EFFECTS AND CONTRAINDICATIONS: Occasional skin rash and urticaria, rarely stomatitis or monilia infections, very rarely an anaphylactic reaction.

DOSAGE: In acute infections, from 125 mg. (200,000 units) 3 times daily to 250 mg. (400,000 units) every 4 hours; for prophylactic use, 125 mg. (200,000 units) once or twice daily. Children under 12 receive dosage in proportion to age and weight.

PREPARATIONS: Soluble granules, cherry-flavored, when reconstituted; 125 mg. per 5 ml. when diluted according to directions.

PACKAGING: 1 Gm. in 40 ml. containers and 2 Gm. in 80 ml. containers.

SUPPLIER: Abbott Laboratories.

Cyclospasmol

GENERIC NAME: Cyclandelate.

INDICATIONS: Orally effective peripheral vasodilator and spasmolytor, indicated in vasospastic and obliterative disorders, including intermittent claudication, leg ulcer and Raynaud's disease.

DOSAGE: 100 mg. four times daily.

PREPARATIONS: Tablets of 100 mg.

PACKAGING: Bottles of 100 tablets.

SUPPLIER: Ives Cameron.

Kenalog

GENERIC AND CHEMICAL NAMES: Triamcinolone acetonide; the acetonide of 9-alpha-fluoro-16-alpha-hydroxy-prednisolone.

INDICATIONS: Anti-inflammatory, antipruritic, and antiallergic.

SIDE EFFECTS AND CONTRAINDICATIONS: Systemic toxicity, such as edema and electrolyte imbalance, has not been observed even though some patients were purposely given massive topical doses.

DOSAGE: Cream and lotion—apply to affected area 2 to 3 times daily and rub in; ointment—apply a thin film 2 to 3 times daily.

PREPARATIONS: 0.1% cream, lotion, and ointment.

PACKAGING: Cream and ointment—5 Gm. and 15 Gm. tubes; lotion—15 ml. plastic squeeze bottles.

SUPPLIER: Squibb.

Lipomul I.V.

COMPOSITION: Cottonseed oil, dextrose anhydrous, lecithin, and oxyethyleneoxypropylene polymer.

INDICATIONS: In patients unable to take adequate food by mouth for any considerable period of time, i.e. malnourished patients, patients whose gastrointestinal tracts are not functioning properly, extensive burn cases, in traumatic conditions severe enough to cause debilitation and prolonged convalescence, patients with gastrointestinal disease, and in certain patients with acute or chronic renal failure in whom a maximum nitrogen-sparing effect is indicated.

SIDE EFFECTS AND CONTRAINDICATIONS: Must not be mixed with blood or any other infusion fluid or drug, or given simultaneously through the same tubing. Use only recipient set supplied with Lipomul I.V.

DOSAGE: Intravenously, not more than 2 units of 500 ml. daily, with total not to exceed 14 infusions. Infants and children, maximum daily dose ranges up to 10 ml. per pound of body weight.

PREPARATIONS: Fat emulsion containing cottonseed oil 15 Gm., dextrose anhydrous 4 Gm., lecithin 1.2 Gm., and oxyethyleneoxypropylene polymer 0.3 Gm., in 500 ml.

PACKAGING: Bottles of 600 ml. containg 500 ml. of 15% fat emulsion, with sterile recipient set.

SUPPLIER: Upjohn Co.

Hydeltrasol Injection

GENERIC NAME: Prednisolone 21-phosphate, as di-sodium salt.

INDICATIONS: Has same intrinsic properties as prednisolone and can produce the same hormonal effects. For emergency and general use wherever corticosteroid therapy is indicated; in such conditions as severe allergic reactions, status asthmaticus, acute non-surgical shock, adrenal insufficiency, and acute life-threatening infections.

SIDE EFFECTS AND CONTRAINDICATIONS: Side effects most commonly associated with prolonged systemic adrenocortical steroid therapy; most important precaution is an evaluation of relative contraindications to steroid therapy such as diabetes mellitus, psychotic tendencies, osteoporosis, hypertension, peptic ulcer, etc.

DOSAGE: Intramuscularly or intravenously, 20 to 100 mg., repeated as necessary, but not exceeding 400 mg. daily. For constant maximal effect, dosage must be repeated at 3 or 4 hour intervals.

PREPARATIONS: Injection 20 mg. per ml.

PACKAGING: Vials of 2 ml. and 5 ml.

SUPPLIER: Merck Sharp & Dohme.

Ilosone

GENERIC NAME: Erythromycin ester as the propionate.

INDICATIONS: Bacterial infection; antibacterial potency of blood concentrations is three times greater than that obtained with the coated tablets; potent therapeutic levels attained within 30 minutes and sustained several hours longer.

DOSAGE: Usually, 0.25 Gm. every 6 hours.

PREPARATIONS: Capsules of 0.125 Gm and 0.25 Gm.

PACKAGING: Bottles of 24 and 100 capsules.

SUPPLIER: Lilly.

Madribon

CHEMICAL NAME: 2,4-Dimethoxy-6-sulfanilamide-1,3-diazine.

INDICATIONS: Antibacterial useful in upper respiratory infections, such as tonsillitis, pharyngitis, pneumonia, sinusitis, otitis media and bronchitis, when due to susceptible organisms; also urinary tract, systemic and soft tissue infections; used prophylactically against meningitis, rheumatic fever, and secondary invaders in virus infections.

DOSAGE: Adults, 1 Gm. initially and 0.5 Gm. daily thereafter; children, 0.25 Gm. per 20 lbs. body weight initially, followed by one-half the initial dose every 24 hours thereafter.

PREPARATIONS: Suspension 0.5 Gm. per 5 ml. and tablets of 0.5 Gm.

PACKAGING: Bottles of 4 and 16 ounces of suspension, and bottles of 30, 250 and 1,000 tablets.

SUPPLIER: Roche Laboratories.

Orabilex

GENERIC NAME: 3(3-Butyrylamino-2,4, 6-triiodophenyl)-2-ethyl sodium acrylate.

INDICATIONS: Oral cholecystographic medium for roentgenographic visualization of the gallbladder and biliary ducts; facilitates interpretation of x-ray films by avoiding production of confusing intestinal opacities; minimizes incidence of gastrointestinal tract reactions and dysuria; increases incidence of biliary duct visualization.

DOSAGE: Six capsules, to be taken approximately 12 to 14 hours before examination.

PREPARATIONS: Capsules of 0.75 Gm.

PACKAGING: Envelopes of 6 capsules, in boxes of 5, 25 and 100 envelopes and in bottles of 250 capsules.

SUPPLIER: E. Fougera.

Parafon
Parafon with Prednisolone

COMPOSITION: Chlorzoxazone and acetaminophen (Tylenol), with or without prednisolone.

INDICATIONS: Long-lasting relief in most disorders involving skeletal muscle spasm. With prednisolone, anti-inflammatory action of the steroid is combined with the muscle relaxant and analgesic properties of Parafon.

DOSAGE: Two tablets 3 times daily.

PREPARATIONS: Parafon—scored, pink tablets containing 125 mg. chlorozoxazone and 300 mg. acetaminophen; Parafon with Prednisolone—contains, in addition, 1 mg. prednisolone.

PACKAGING: Parafon—bottles of 50 tablets; Parafon with Prednisolone—bottles of 36 tablets.

SUPPLIER: McNeil Laboratories.

Sterotril

COMPOSITION: Prednisone (Meticorten) and perphenazine (Trilafon).

INDICATIONS: Antirheumatic and anti-inflammatory together with stress-countering action of perphenazine; for rheumatoid arthritis and other related rheumatic diseases, allergic and inflammatory dermatoses, bronchial asthma, and similar conditions.

SIDE EFFECTS AND CONTRAINDICATIONS: The same contraindications which apply to corticosteroids and phenothiazines when given separately apply to Sterotril.

DOSAGE: Dosage depends on severity and prognosis. Acute conditions or initial suppressive therapy, 2 tablets 3 or 4 times daily; maintenance dosage, 1 tablet 4 times daily.

PREPARATIONS: Tablets containing prednisone 2.5 mg. and perphenazine 2 mg.

PACKAGING: Bottles of 30 and 100 tablets.

SUPPLIER: Schering Corp.

Trancopal

GENERIC NAME: Chlormethazanone.

INDICATIONS: In disorders characterized by skeletal muscle spasm such as low back pain, neck pain (torticollis), bursitis, rheumatoid arthritis, etc.; in psychogenic disorders including anxiety and tension states, dysmenorrhea, premenstrual tension, asthma and angina pectoris.

DOSAGE: Adults, 100 mg. 3 or 4 times daily; children, one-half the adult dosage.

PREPARATIONS: Capsules containing 100 mg. of chlormethazanone.

PACKAGING: Bottles of 1,000 capsules.

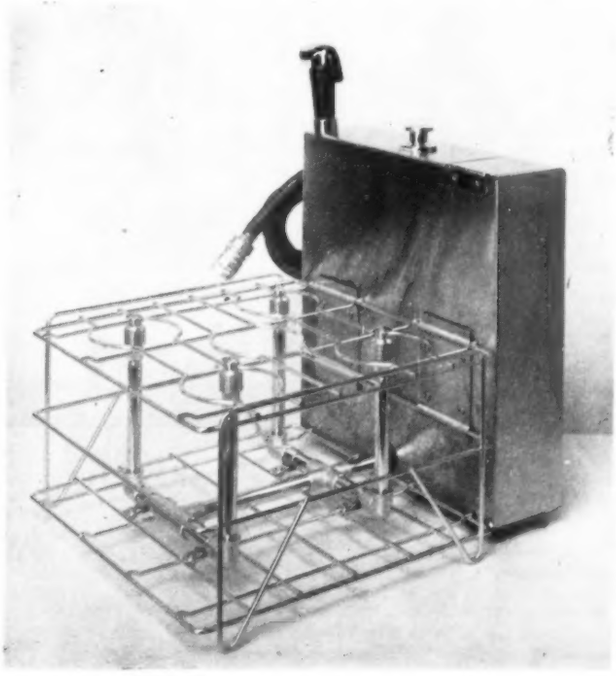
SUPPLIER: Winthrop Laboratories.

Notes + Suggestions

edited by CLIFTON J. LATIOLAIS

FLASK WASHER

The Model FW-4 Portable Flask Washer* is a four place flask washer, designed for portable installation on a sink. Dimensions are 14″ x 16″ x 5″; other models are available. The water inlet hose may be attached to a hot water faucet. An automatic detergent dispenser injects liquid detergent into the water line. A hose with spray head is supplied for



rinsing flask exterior. Flasks cleaned in this washer must be removed for rinsing with freshly distilled water.

An accessory device is available to convert the FW-4 from a flask to a vial washer. This attachment accommodates vials from 5 ml. to 100 ml. capacity.

*The Macbick Company, 243 Broadway, Cambridge, Mass.

NAXOL BULLETIN

The 31-page Technical Bulletin I-20-Naxol* describes the physical and chemical properties and suggested uses of cyclohexanol. Cyclohexanol is used for its homogenizing and stabilizing effects in disinfectant solutions. Cyclohexyl metaborate is used as a hygroscopic agent for both cosmetic and medicinal skin preparations. Cyclohexanol is used in waxes, and polishes due to its blending and emulsifying properties.

*Available from National Aniline Div., Allied Chemical and Dye Corp., 40 Rector St., New York 6, N. Y.

AMPUL SEALER

The new ampul sealing machine, Model HS-1* is a table model, motor driven sealer, designed for small production runs. The sealer will handle all types of glass ampuls ranging in size from 1 ml. to 20 ml. Special adapters are available for larger size ampuls. Ampuls can be sealed at rates of approximately 500 to 1,000 per hour.

Glass ampuls are guided into position manually between rotating rollers. The glass may be tip sealed or pull sealed. Oxygen and gas are controlled by two small needle valves. The motor operates on 110 V AC. Overall dimensions of the sealer are 10″ long by 7″ high by 15″ deep, and weighs 7½ pounds.

*Available from Popper and Sons, Inc., 400 Fourth Ave., New York 10, N. Y.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

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edited by CLIFTON J. LATIOLAIS *and* LEO F. GODLEY

VITAMIN D. SPECTROPHOTOMETRIC DETERMINATION OF

Some Paper - Chromatographic Studies on Vitamin D, Mayer, A., Picard, C. W. and Wokes, F., Pharm. Acta Helv. 33:603 (Aug.-Oct.) 1958.

The use of paper chromatography as a means of separating small quantities of vitamin D for subsequent spectrophotometric estimation has been studied with a view to developing a physicochemical method of estimating vitamin D in body fluids.

It has been found that the instability of vitamin D (ergo- and cholecalciferols) is markedly accentuated on exposure in high alcoholic dilutions or in spots on paraffin-impregnated filter paper. The main causative factors have been investigated and precautionary measures are suggested to minimize this instability, which has however not yet been overcome for the micro-quantities requiring measurement in body fluids.

The formation of various degradation products has been established and followed by spectrophotometry before and after development of the chromatograms.

Experiments with cholecalciferyl-4 C^{14} butyrate indicated that its low recoveries as measured by Geiger counts were similar to those measured spectrophotometrically, suggesting that incomplete elution can be a further factor affecting the recovery.

The findings are discussed with special reference to the photochemical transformation of provitamins D involving precalciferol. Problems requiring further investigation are indicated.

AUTHOR'S SUMMARY

SUPPOSITORIES, INFLUENCING RESORPTION OF SULFONAMIDES FROM

Influencing the Resorption of Rectally Administered Drugs by Means of Suppository Bases, Pennati, Von L. and Steiger-Trippi, K., Pharm. Acta. Helv. 33:663 (Aug.-Oct.) 1958.

To achieve high blood levels following rectal application, the sulfonamides must be as soluble in water as possible. Very slightly water-soluble sulfonamides provide higher peak blood levels with water-soluble suppository excipients than with fat-soluble excipients.

The highest blood concentration-time products, and the highest blood level values, were obtained with the freely water-soluble sulfasomidine sodium in Massuppol®, a fatty excipient containing an emulsifier.

AUTHOR'S SUMMARY

SUPPOSITORIES, DRUG RELEASE FROM

The Influence of Certain Properties on Drug Release from Suppository Masses, Eckert, Von V. and Mushlemann, H., Pharm. Acta. Helv. 33:649 (Aug.-Oct.) 1958.

If a drug dissolves in a suppository base, release and intestinal absorption are much slower and more continuous than in the presence of a suspension.

Release of a drug insoluble in a fat-like suppository base, but soluble in water (procaine HCl), depends upon the melting state and the interval between the moment when the specimen begins to expand and the moment the melted mass is cleared. Below the clear melting point, release is insignificant. At the clear melting point and above, the rate of release increases enormously, and the rate of diffusion reaches the values of a corresponding aqueous solution. Excipients with great melting interval are less favorable than those with small melting interval.

Hydrophilia of the base has no significant influence, provided the hydroxyl number does not exceed 50.

Release of a drug (aminopyrine) soluble in fat-like bases is only slightly affected by the melting state. Occasionally, an evident increase was observed after reaching the clear melting point. On the whole, much less drug is released per unit of time than by a drug which is insoluble in the suppository base (procaine hydrochloride).

In contrast to a drug insoluble in fatty base, release of a drug soluble in such an excipient is markedly influenced by hydrophilia, the release being slowed down as the hydroxyl number increases.

Water soluble bases (G2151) always release the drug less quickly than fatty bases, independently of the melting state. Consequently, a fat-like base should have[1] a clear melting point not exceeding about 36.5 deg. C.,[2] as small a melting interval as possible, and[3] as small an hydroxyl number as possible.

When a quick effect is required, a fatty base should be used in which the drug is insoluble and in which the drug must be incorporated in the form of a suspension. If the effect is to be delayed, a base should be chosen in which the drug is soluble.

AUTHOR'S SUMMARY

OINTMENTS, EFFECT OF PROTEIN HYDROLYSATE

The Influence of Ointments Containing Protein Hydrolysate on Experimental Wounds, Heite, Von H. J. and Muller - Nieworth, S. E., Arzneimittel Forchung 8:595 (Sept.) 1958.

A recently devised experimental model for testing the effect of ointments promoting wound healing has been used to investigate the influence of ointments containing aqueous solutions of different osmotic concentrations together with protein hydrolysates on wound healing. The model procedure consists of continuous recordings and bilateral comparsion of the healing rates in punched wounds applied to x-rayed areas of the rabbit's ear. Evaluations were performed by variance analyses with observation of the following features: (a) inclination of the healing curve, i.e. the regression coefficient. (b) degree of healing attained (residual diameter of punched wounds) at the point of termination of the experiment (i.e. after one ear wound has completely healed in 50% of the animals).

Under the influence of ointments containing hypotonic or hypertonic NaCl solutions, wound healing proceeds slower than in animals treated with blood-isotonic saline concentrations. This may be explained by disturbance of exchange processes occurring between the capillaries and interstitial space. The pH of the ointments, which was kept at the values 6.2, 7.2 and 8.3 by addition of 3 isotonic phosphate buffers, showed no significant influence on the rapidity of wound healing.

Ointments containing protein hydrolysates were found to be significantly more effective than hydrolysate-free ointment bases. The stimulation of wound healing through protein hydrolysates was most marked in neutral buffered ointments. The stimulation of wound healing by protein hydrolysates may also serve to explain the well-known favorable effects of preparations containing trypsin and of exposition of the wound to dressings soaked in wound secretions for several days.

AUTHOR'S SUMMARY

BARBITURATES, DETECTION REACTIONS OF

Detection Reactions of Barbiturates, Jokl, V. and Janeckova, E., Ceskoslov. Farm., 7:397 (July) 1958.

Selective detection of barbiturates and hydantoins is based on Zwikker's reaction. The chromatogram is immersed into solution of $[Cu(pyridine)2]^{2+}$ and then into diluted solutions of disodium salt of ethylenediamine tetraacetic acid which suppresses the interfering background. The spots are detected by immersing the chromatogram into solution of sodium diethyldithiocarbamate. The detection has sensitivity 5 mg. as drop reaction, after chromatography 10 mg. barbiturate. Impregnation of paper with buffer solution does not interfere. Thiobar-

biturates react in the same way. 1-Alkyl substituted derivatives do not give the reaction. Derivatives of uracil give a positive reaction.

AUTHOR'S SUMMARY

RESORCINOL, POLAROGRAPHIC DETERMINATION OF

Polarographic Determination of Resorcinol, Davidek, J. and Manousek, O., Ceskoslov. Farm. 7:399 (July) 1958.

A new polarographic method is described for the determination of resorcinol. Because of its specificity and sensitivity the method is suitable for determination of resorcinol in pharmaceutical preparations. It is based on the polarographic determination of 2,4-dinitroresorcinol resulting from nitrosation of resorcinol in acid medium following the addition of alkaline nitrite. The method is accurate to within 3 to 4 percent.

AUTHOR'S SUMMARY

PLASTIC USED FOR PARENTERALS

Leaching and Sorption of Plastic Used for Parenterals, Autian, J., Bull. Parenteral Drug Assoc. 12:17 (Sept.-Oct.) 1958.

Plastic syringes are usually composed of polystyrene, polyethylene, polymethacrylate, and nylon; plastic tubing of polyethylene or polyvinyl polymers. Additives may be added, possibly up to 1%, to improve the physical or chemical properties of the polymer.

"Leaching," a complex phenomenom whereby additives or trace quantities of unknown compounds are released from the plastic into the liquid medium, can potentially give an untoward reaction in the patient and cause deleterious effects upon the active constituent in the parenteral solution. The process is dependent upon (1) composition of the plastic, the functional groups, and additives; (2) type of solution; (3) solubility of the plastic material in the solvent; (4) temperature; and (5) time of contact. Another phase of the plastic problem is the ability of the plastic substance to take up by chemical or physico-chemical means the active constituents of the parenteral solution. The potency of medical agents or preservatives may thus fall below critical concentrations.

With the present industrial standards and lack of suitable standards of plastics for pharmaceutical use, control procedures become necessary to include physical, chemical and biological testing of the various parenteral solutions with each plastic formulation when the product is to be packaged in a plastic container or cartridge. The problem will become more intensified with the introduction and general use of disposable syringes and tubing.

NORMAN HO

PYRROLIDINO-METHYL-TETRACYCLINE, REVERIN

The Aminomethylisation of the Tetracyclines: Chemistry of Reverin, Seidel, W., Sorder, A., and Lindner, E., Muenchener Medizinische Wochenschrift, 100:661(17) (April) 1958.

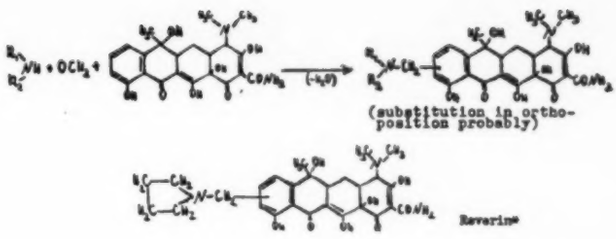
Authors report about experiments of transformation of the tetracycline molecule, experiments designed to make it water-soluble by decisively changing the isoelectric point of the substance, without thereby changing the specific efficiency of the molecule.

Ethers and acetals of the tetracycline could not be formed to satisfaction. Different esters were obtained, but after a short time the free tetracyclines separated in aqueous solution due to hydrolysis.

Only the experiments leading to aminomethylisation of the tetracyclines were successful. By chemical reaction with formaldehyde and proper amines, basic groups could be induced in great variety into the tetracyclines. Excellent water-soluble products resulted, and the water-solubility extends over the whole pH scale, in particular over the important physiological pH range, starting with the tetracycline itself and also with the 5-hydroxy-tetracycline and 7-chlor-tetracycline.

The process of the aminomethylisation of the tetracycline may be pictured as depicted in column two.

Reverin was chosen amongst the many aminomethyl-compounds of the tetracyclines due to its favorable qualities in particular: (1) It is, like tetracycline, an amphoteric substance and therefore able to form salts with bases as well as with acids. (2) The pH of an aqueous solution may be adjusted to any desired value due to this formation of salts; parenteral solutions have



Reverin*

a pH of 5.0 due to the addition of small quantities of organic acids; such solutions will not change color if exposed to open air for many hours: (3) The pI value is around 7.9 (tetracycline 4.3). (4) The solubility in water amounts to 1250 mg./ml., 2500-fold that of the tetracycline. (5) The substance has, like the tetracyclines, a considerable complex-forming capacity. (6) The stability in temperature of Reverin solutions (using water for injection as solvent) shows no difference from those of chlortetracycline in regard to the biological effect under various temperatures (from +5° C. to +100° C.).

Reverin represents the first time a product has been developed by extensive partial-synthesis from a natural antibiotic. This product offers considerable advantages for practical, and particularly for parenteral, use since the therapeutic efficiency-spectrum remains unchanged: (1) It causes no or almost no pain after I.M. administration. (2) It allows rapid and direct I.V. administration (250 mg. in 10 ml. water for injection injected within 1 to 3 minutes) without local damage to the vein at site of injection. (3) It eliminates need for oral administration, thus avoiding therapeutic disadvantages, such as insufficient blood levels, enterocolitis etc.

OTMAR M. NETEZER

*Reverin is pyrrolidino-methyl-tetracycline 'Hoechst'.

ASPIRIN, ASSAY OF

Assay of Acetylsalicylic Acid in Tablets by Non-Aqueous Titration, Kavarana, Homi H., Indian J. Pharm., 20:268 (Sept.) 1958.

Compared with the official method in the *U.S.P.* or *B.P.*, as well as colorimetric methods, non-aqueous titration of aspirin with standard sodium methoxide solution is simpler and more rapid.

The non-aqueous titration method is based on the principle that some organic acids, including acetylsalicylic acid, can be titrated in anhydrous pyridine with sodium methoxide as reagent and phenolphthalein in methanol as indicator. Tablet excipients, as well as other ingredients usually associated with aspirin, such as caffeine, phenacetin, phenobarbital and quinine sulfate do not interfere with the test.

The procedure outlined by the author is as follows. (1) Dissolve about three grams of freshly cut sodium metal in 50 ml. of methanol. Add 100 ml. of methanol and 750 ml. of benzene. (2) Weigh the tablet powder (equivalent to 100 mg. of aspirin) and transfer quantitatively into a 250 ml. iodine flask with the aid of 20 ml. of pyridine and dissolve. Add 4 drops of phenolphthalein (a 1% solution in methanol) as indicator. Titrate accurately with the sodium methoxide solution until the color changes to a distinct pink (color permanent for at least one-half minute). (3) Weigh accurately 100 mg. of pure standard aspirin and transfer quantitatively into a 250 ml. iodine flask. Add 20 ml. of pyridine and dissolve the aspirin. Add 4 drops of phenolphthalein solution as indicator. Titrate accurately as before with sodium methoxide solution to a permanent distinct pink color. (4) Calculate the aspirin equivalent per ml., of sodium methoxide solution and using this factor determine the control in the sample from the first titration value.

CLIFTON J. LATIOLAIS

PHARMACEUTICAL TEACHING BY CORRESPONDENCE

Experiences of the Department of Pharmaceutical Teaching by Correspondence at the Pharmaceutical School of Ulyianovsk, Kaganov, Ju. E., Aptechnoe Delo (U.S.S.R.) 7:41 (July-Aug.) 1958.

During the past year, the pharmaceutical school of Ulyianovsk in the U.S.S.R. has inaugurated a pharmaceutical correspondence course for persons who are professionally

active in pharmacies but who do not possess the diploma. The best professors of the school have been designated to teach this course. As preliminary education, all students shall have finished their studies at a high school. The pharmaceutical correspondence course will last three years. Special plans for the study of botany, analytical chemistry, anatomy, physiology, technology, pharmaceutical chemistry, organic chemistry, etc. have been or will be formulated by professors of the various departments. Each student will be required to submit comprehensive themes on the various subject studied before they are allowed to take the examinations. Prior to the examinations, the students will assemble in Ulyianovsk where they will attend summarizing lectures and hold consultations with the professors.

Although there are still many problems in connection with pharmaceutical teaching by correspondence to be solved, present experiences indicate that the course will fulfill its purpose, *i.e.* to educate pharmacists with a qualification which is equivalent to that obtained by normal studies.

HUBERT ZACEK

OPHTHALMIC SOLUTIONS

Rational Basis for the Preparation of Ophthalmic Solutions, Riegelman, S. and Vaughan, D.G., Am. Profess. Pharm. 24:757 (October) 1958.

The author opens with a discussion of the most important factors to consider in preparing ophthalmic solutions. They are tonicity, hydrogen ion concentration, stability, viscosity, selection of a preservative, and sterility.

This is followed with a discussion of certain recommendations for the preparation of ophthalmic solutions. All drugs used in injured eyes should be compounded with 2.0% boric acid solutions, with the exception of alkaline drugs which should be in sterile distilled water. Solutions to be used during surgery should be filtered and should not contain preservatives as they are irritating to the inner eye structure. All such solutions for use on eyes that have been traumatized by injury or surgery should be packaged in single-patient containers and autoclaved for 15 minutes at 15 pounds pressure.

Solutions intended for use in eyes with an intact corneal epithelium may be packaged in multiple dose containers. All drugs except the alkaline ones and pilocarpine salts should be compounded in normal saline or preferrably 2.0% boric acid solution. The pilocarpine salts for home use should be compounded in the phosphate buffer and alkaline drugs in preserved water (parasepts). Stock solutions of these vehicles containing preservative should be available. The stock vehicles should be autoclaved at 15 pounds pressure for 15 minutes and stored in autoclaved, sealed, moderate volume containers. Bacterial filtration may be used if there is no chance of introducing previously filtered drugs into the ophthalmic solution. Once the seal on a stock bottle of the vehicle is broken, it should be used within 24 hours.

DOUGLAS SILVERNALE

ANTIBIOTIC PATENT

Antibiotic Preparations, Hans Jacobsen (to Novo Terapeutisk Laboratorium A/S), Brit. 792,545, Mar. 26, 1958.

Finely pulverized antibiotics coated with 1-5% of an aluminum salt of a fatty acid and suspended in oil provide prolonged effects upon injection. Thus, aluminum monostearate 16 was dissolved in trichloroethylene 385 and mixed with ground procaine penicillin 320 Gm. Trichloroethylene was removed by evaporation and, the powder disintegrated and suspended in sesame oil to make 1,000 ml. The suspension was homogenized and treated *in vacuo* at 1 mm. and 30-40° for three hours.

JOACHIM ANSCHEL, CHEMICAL ABSTRACTS 16702h

VITAMIN B_{12}, STABILIZATION

Stabilization of Vitamin B_{12} in Pharmaceutical Preparations, Ponci, R., Farmaco (Pavia), Ed. Prat. 13:71, 1958. Italy.

Various methods are discussed with six references. A satisfactory solution consists of 0.4 gamma of vitamin B_{12}, 20 mg. of ascorbic acid, 17 mg. ferrous gluconate ml. in a vehicle of 70% sorbitol solutin brought to a pH 4 with sodium citrate. The preparation, kept for one year at 25°, lost 20% of vitamin B_{12} and 19% of the ascorbic acid. An overdosage of 25% of both vitamins is recommended.

A. E. MEYER, CHEMICAL ABSTRACTS, 17618d

STERILIZATION OF LOCAL ANESTHETICS

Is Heat Sterilization of Local Anesthetic Drugs A Necessity? Bridenbaugh, L. Donald, Moore, Daniel C., J. Am. Med. Assoc. 168:1334 (Nov. 8) 1958.

The assurance that a local anesthetic solution as well as the equipment employed for its injection is free from contamination prior to performance of a regional block procedure has always been of concern to the physician using these techniques. Heat sterilization of the equipment is a standard procedure. Unfortunately, the misconception that the potency of drugs used to prepare local anesthetic solutions is markedly decreased by heat sterilization and the assumption that such drugs or solutions are sterile as received from the pharmaceutical firm commonly results in cold sterilization or no resterilization of the drugs prior to use. The authors sent a questionnaire to all hospitals in the state of Washington in August 1957 pertaining to techniques observed in using local anesthetic drugs. Only 33 out of 101 hospitals were autoclaving the solutions before use. The remaining 68 hospitals depended on cold sterilization techniques. Clinical experience with 17,368 regional block procedures has convinced the authors that a careful technique involving the autoclaving of the local anesthetic solution in its container is mandatory. The commonly used local anesthetics are autoclaved at 124° to 127° C. and 18 to 20 pounds pressure without significant loss of potency to alter the expected clinical results. Therefore, the danger of bacterial contamination is reduced and the danger of antiseptic solution entering a cracked ampul is eliminated.

A. GORDON MOORE

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION
—Purchasing

Skolaut, Milton W.: How the Pharmacist Can Help Solve Problems in Purchasing Medical Supplies, *Hospitals* 32:61 (Nov. 1) 1958.

DISASTER PREPAREDNESS

Sister Mirian Thomas: Preparedness Pays When Disaster Strikes, *Hosp. Topics* 36:31 (Nov.) 1958.

LAWS AND REGULATIONS

Milne, W. M. and Fears, N.: Hospital Pharmacy Controls, *The Hospital Pharmacist* (Canada) 11:239 (Sept.-Oct.) 1958.

PHARMACY AND THERAPEUTICS COMMITTEE
(includes hospital formulary duplication and detailing)

Wagner, George N.: Friendly Controversy, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 19:602 (Oct.) 1958.

RECRUITMENT
—Hospital Pharmacy

Holt, David H.: A Pharmacy Student Recruitment Program, *Hosp. Management* 86:102 (Dec.) 1958.

SAFETY PROCEDURES

Sister Ste. Rose, s.g.c.: Caution, Danger, Death, *Hosp. Progress* 39:108 (No.) 1958.

STANDARDS

Zugich, John J.: Substandard Practices, *Am. Profess. Pharm.* 24:860 (Nov.) 1958.

GENERAL

Nichols, Terry B.: The Pharmacist's Twin Roles, *Hospitals* 32:49 (Dec. 1) 1958.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to Oct. 18, 1958.

Notice

New and Nonofficial Drugs 1958 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1958 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to January 1, 1958. The index listed below contains those drugs evaluated and published between January 1, 1958 and October 18, 1958.

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Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary*

USE OF DRUGS IN SHOCK ACCOMPANYING MYOCARDIAL INFARCTION

Arthur Selzer, M.D. and David A. Rytand, M.D., San Francisco

► SHOCK IS ONE of the most dreaded sequels of acute myocardial infarction. Its mortality rate, estimated at above 80%, is approximately three to four times higher than the over-all mortality of acute myocardial infarction, as based on unselected series, and more than 20 times higher than some "good-risk" series. With arrhythmias and thromboembolic phenomena, it constitutes a triad of complications of myocardial infarction, the elimination of which would tremendously improve the prognosis of a single attack.

From the Department of Medicine, Stanford University School of Medicine.

Within the past decade the therapeutic approach to shock accompanying myocardial infarction has changed from passive and symptomatic treatment to an active and vigorous use of drugs including blood volume expanders. The evaluation of such therapy and the establishment of a clear-cut policy are difficult for two reasons. In the first place, the causes and mechanism of this form of shock are not well understood. Secondly, the extreme seriousness of this condition precludes all but the simplest methods of objective circulatory studies. This report attempts to evaluate critically the present status of drug therapy of shock associated with acute myocardial infarction.

Nature of Shock Accompanying Myocardial Infarction

Shock may be defined as a clinical syndrome associated with a physiological state in which the circulating blood volume is disproportionately small for the size of the vascular bed. Shock thus arises when blood pressure necessary for the perfusion of important organs cannot be maintained. It is, therefore, a failure of the peripheral circulatory regulation system, and the abnormally low cardiac output characteristic of shock is ordinarily a phenomenon secondary to inadequate venous return to the heart. On the other hand, the heart may, under certain circumstances, become the principal cause of shock, in which case shock becomes primarily cardiac, or "cardiogenic" in origin. The concept of cardiogenic shock implies that the heart is incapable of maintaining adequate output for the sustenance of a reasonable blood pressure in spite of an adequate venous return.[1] There are two clinical syndromes in which this appears to be the case, pericardial tamponade and tachycardias with intolerably rapid ventricular rates. In both of these conditions the clinical picture of shock may appear, often accompanied by signs of congestive failure. In neither of these syndromes is failure of the myocardium present; in the one, a high intrapericardial pressure and, in the other, a short diastole interfere with diastolic filling of the heart and so produce critical fall in cardiac output. Massive myocardial infarction may destroy enough of the functioning myocardium as to produce sudden left ventricular failure severe enough to cause shock.

It would seem obvious that, in myocardial infarction, the peripheral factor and the cardiogenic factor may both be present and, in part, may be responsible for each other. Pain and tissue destruction in general, including myocardial infarction, are shock-producing factors by way of the peripheral mechanism. On the other hand, the inadequate coronary perfusion resulting from prolonged hypotension may bring about cardiac failure or even myocardial infarction. Shock complicating myocardial infarction could thus be considered to involve a vicious circle, wherein it would be impossible to determine the principal initiating mechanism.

The two opposing concepts of shock secondary to myocardial infarction are of considerable practical importance. If it is established that this form of shock is primarily neurogenic in origin, then the purpose of therapy would be to maintain or restore arterial pressure by the use of purely peripherally acting pressor drugs. If, on the other hand, this form of shock is entirely a manifestation of cardiac failure, then peripheral pressor effect would constitute an additional overload upon the already incompetent, overstretched heart and would be highly undesirable. In this case, drugs with cardiotonic effect would be helpful.

Both clinical and experimental studies have contributed little to the understanding of shock secondary to myocardial infarction. Circulatory measurements in even milder cases of myocardial infarction have demonstrated some elements of failure, such as lowered vital capacity, prolonged circulation time,[2] and increased venous pressure.[3] The cardiac output tends to be low in myocardial infarction,[4] with patients in shock showing, as a rule, lower values than those not in shock. These observations are, however, insufficient to establish cardiac failure as the primary cause of shock. Experimentally, cardiogenic shock has been reproduced by massive destruction of the myocardium[5] or by severe overloading of the right ventricle,[6] but shock can also be produced by peripheral mechanisms.[7]

Bedside observations in patients with acute myocardial infarction indicate that, if circulatory disturbances appear clinically in the course of acute myocardial infarction, they are likely to present themselves at first as pure cardiac failure (orthopnea, pulmonary edema, gallop rhythm, pulsus alternans, and congestive phenomena) or as pure shock (restlessness, cold perspiration, ashen cyanosis, tachycardia, and evidence of intense vasoconstriction). The combination of both syndromes is considerably less common than the appearance of either one alone, and a picture of severe cardiac failure associated with severe shock in a patient is usually a terminal event.

The variability in the clinical picture of shock presents the possibility that shock accompanying myocardial infarction may be caused by different mechanisms in different cases.[8] The following good arguments can be advanced against the theory that a single pathogenic factor causes shock in myocardial infarction: (1) the aforementioned variety of clinical patterns of shock secondary to myocardial infarction; (2) the occasional successful reversal of shock by the elimination of such diversified contributory factors as severe pain in some cases and cardiac arrhythmias in others; and (3) reports by careful observers of partial or complete relief of shock secondary to myocardial infarction by the use of agents having directly opposite actions upon the circulatory system, such as phlebotomy, on the one hand,[9] and blood transfusions, on the other,[10] or digitalis[11] and peripherally acting pressor amines.[12]

It was, therefore, suggested that the early shock which develops immediately after the initial attack may be of the nature of reflex vasomotor collapse, whereas the late shock, characterized by gradual onset and often accompanied by some evidence of cardiac failure, suggests cardiogenic mechanism.[8] Between these two "pure" forms of shock, there may be many intermediate and combined forms.

Indications for Therapy

The fall in blood pressure which frequently accompanies myocardial infarction has two effects upon the heart, the favorable effect of lowering the work of the damaged organ and the unfavorable one of reducing the perfusion pressure in the coronary circulation. The latter may be of particular importance, in that higher perfusion pressure might provide some collateral blood supply to the damaged areas. It may be assumed that the two opposite factors balance each other under ordinary circumstances. The appearance of the clinical manifestations of shock suggests that arterial pressure has fallen below the critical point of perfusion of important organs, including the heart, and that higher pressure may be necessary, regardless of its increased work load on the heart. Probably the fall in blood pressure that often follows acute myocardial infarction is, in part at least, a manifestation of a homeostatic mechanism which attempts to set the work of the heart at an optimal level. It would follow that the establishment of an arbitrary danger level of blood pressure is unsound. An expectant conservative attitude can be recommended even in the presence of systolic pressure as low as 80 mm. Hg, provided that none of the signs of shock are present, that the patient's urinary output is adequate, and that the heart rate is not unduly rapid. On the other hand, signs of shock may appear in a patient who had hypertension prior to the attack, even though the systolic pressure may be 120 mm. Hg or more; in that case, treatment may be indicated. Thus, the primary indication for treatment is the presence of clinical signs of shock. When shock is present, it is necessary to decide whether to use simple, nonspecific measures or to use antishock therapy. Nonspecific measures, including recumbency, administration of oxygen, and the use of morphine or its substitutes, sometimes correct the early shock which may be a manifestation of simple stress, apprehension, or nausea, or which may be a form of vasovagal collapse. If shock is of overwhelming severity or if it does not respond to nonspecific measures within a reasonable time, then more specific antishock therapy should be undertaken. Such therapy should be considered a major therapeutic maneuver and itself carries a definite risk.

In some cases, shock secondary to myocardial infarction may be associated with the presence of various forms of cardiac arrhythmias, which may be assumed to contribute to the state of shock. These include rapid cardiac rhythms, such as paroxysmal tachycardias, atrial flutter or fibrillation with uncontrolled ventricular rates, on the one hand, and higher degrees of heart block with slow ventricular rates, on the

other. In the presence of circulatory embarrassment, even minor disturbances of rhythm, such as brief periods of bigeminal rhythm, could contribute to heart failure or shock. This is suggested by the fact that even a single premature beat can be followed by the appearance of mechanical alternation of the pulse for a period of several beats. Therefore, a serious effort should be made to eliminate arrhythmias, if possible, before antishock therapy is instituted. In those cases in which shock is associated with obvious evidences of cardiac failure, either left ventricular or combined type, treatment of failure should take precedence over antishock therapy.

Drug Therapy

Pressor Amines.—Sympathomimetic drugs with primary effect on peripheral arterioles are usually referred to as "pressor amines" and are used because of their action in increasing the systemic peripheral arteriolar resistance. Pressor effect is only one of their actions, however, and their effective use in hypotension may be overshadowed by other, undesirable actions. Thus, few of the older sympathomimetic drugs are useful for the treatment of shock. Epinephrine, the most powerful local vasoconstrictor, has a negligible effect on the peripheral vascular resistance. Its pressor effect is, in most part, due to a powerful stimulation of the myocardium and increase in cardiac output. The associated increase in myocardial irritability makes it an unsuitable drug for the treatment of myocardial infarction and cardiac failure. Ephedrine and amphetamine (Amphetamine, Benzedrine, Raphetamine) have an action similar to that of epinephrine, though slower and more sustained, and differ from the latter by being effective orally. These two drugs do not have, however, a dependable pressor effect and are used more for their bronchodilating and cerebrum-stimulating effects, respectively, although ephedrine has been used with equivocal results in the treatment of postural hypotension. Phenylephrine (Neo-Synephrine) was the first pressor amine to be used as a pressor agent during spinal anesthesia because of the predominant action on the cardiovascular system. Similar uses have been applied to hydroxyamphetamine (Paredrine). However, not until levarterenol (Levophed) became available did interest awaken in the use of pressor amines for shock occurring in cardiac patients.

Levarterenol, also known as *l*-norepinephrine, was long suspected of being the adrenergic nerve mediator, since it has been isolated from adrenal medullary extracts. The separation of pure levarterenol from racemic arterenols in 1948 supported the hypothesis of its physiological function and provided a basis for the study of its pharmacodynamic action, which eventually led to its clinical application in the treatment of hypotensive states. Studies by Goldenberg and co-workers[13] have shown that levarterenol administered as a continuous intravenous infusion increases the systemic blood pressure without increasing the cardiac output, therefore significantly raising peripheral resistance. In addition, levarterenol causes significant capillary and venous constriction. It has, furthermore, a direct stimulating effect upon myocardial contractility in the dog.[14] The question as to whether levarterenol enhances undesirable cardiac arrhythmias, a byproduct of the myocardium-stimulating effects of drugs, is still a subject of controversy. Experimental evidence supports, as a whole, the view that the severe arrhythmogenic effect of epinephrine is matched by that of levarterenol.[15] Clinical studies suggest, on the other hand, that therapeutic doses of levarterenol do not frequently precipitate arrhythmias, although some investigators stress the importance of such dangerous complications.[16]

The action of levarterenol in increasing the peripheral resistance in human beings is amply demonstrated, both in normal individuals and in patients with shock.[17] This action makes it admirably suitable in normovolemic and hypervolemic forms of shock.[17a] Levarterenol has been used extensively in shock secondary to acute myocardial infarction.[18] The results of all the earlier studies were interpreted as showing that it has a beneficial effect on shock of myocardial infarction, both in restoring a more normal arterial pressure and in reducing the over-all mortality rate. A significant pressor effect was observed in the majority of cases. The effect upon the mortality rate showed a wide variation, with its reduction to 14% in one small series[19] and with relatively little reduction in others. Recently, reports have appeared denying any beneficial effect whatsoever of levarterenol in shock secondary to myocardial infarction.[20]

A critical evaluation of the effect of levarterenol on cardiogenic shock is rather difficult in view of the contradictory results. The difficulty is, in part, due to the lack of uniformity in defining the state of shock that follows myocardial infarction. The wide range of responses to therapy suggests that different types of patients were treated and compared with each other. Futhermore, the theoretical indications for therapy with levarterenol are not entirely clear. Those investigators who regard shock as a disturbance of the vasomotor mechanism use levarterenol primarily for its peripheral action of increasing arteriolar resistance. Those who believe that shock of myocardial infarction is cardiogenic regard any success from use of levarterenol as largely caused by direct myocardial action.[19] The latter view is based on two observations: (1) the use of levarterenol in patients who exhibited shock and cardiac failure, in whom signs of pulmonary edema and congestive phenomena improved; and (2) the failure to note such an improvement in similar patients treated with phenylephrine, which has a purely peripheral vasomotor effect.[19] These studies bring out the only positive arguments for the existence, in human beings, of a direct myocardium-stimulating effect of levarterenol. Yet these arguments are not entirely acceptable as evidence for such a cardiac effect of the drug. First, improvement of cardiac function could be effected by a pressor effect of the drug, resulting in improvement of coronary perfusion, and, second, the comparison between phenylephrine and levarterenol has been based on a series far too small to permit definite conclusions to be drawn.

Another important and undecided question is the optimal time for the administration of levarterenol. Some workers[18e] stress the importance of an early start of antishock therapy, suggesting that a delay of the onset of treatment for over three hours sharply limits the success and increases the mortality. Yet, if one is to treat shock within the first two hours of its onset, one is sure to include many cases of simple vasomotor collapse which could clear without specific therapy, therefore exaggerating the apparent success of the group treated earlier.

The principal advantage of levarterenol in the treatment of shock lies in its ease of administration. The drug, given by continuous intravenous drip, can take effect within a minute or two and can be instantly withdrawn if it is no longer needed. The pressor effect can easily be titrated by the speed of the infusion or by the concentration of the drug in the solution. Its disadvantage is the local vasoconstrictive effect, which may lead to serious tissue necrosis if extravasation of the drug occurs.

In recent years several other pressor amines have been introduced for the treatment of shock. The three drugs investigated for their effect on shock secondary to myocardial infarction are mephentermine (Wyamine), methoxamine (Vasoxyl), and metaraminol (Aramine).

In experimental animals, mephentermine shows an action similar to that of levarterenol by exhibiting a pressor effect caused by increase in systemic arteriolar resistance and a myocardial-stimulating action. In human beings, it has been used in shock accompanying myocardial infarction, with moderate success.[21] After intramuscular injection a pressor effect lasting up to four hours can be observed, with no significant increase in arrhythmias in the cases studied.

Methoxamine differs from mephentermine and levarterenol in that is shows, in experimental animals, a pure peripheral pressor effect, without exhibiting any myocardial effect. Experimental studies suggest a significantly lower tendency to produce arrhythmias. It is effective by the intramuscular route in intermittent doses.

Metaraminol combines a strong pressor effect with a myocardial-stimulating action in experimental studies.[22] Its

clinical use is similar to that of levarterenol except for the absence of tissue-irritating action; therefore, the drug can be administered both by continuous intravenous drip and by repeated intramuscular injections.[23] Clinical trials of metaraminol for the treatment of shock associated with myocardial infarction showed results comparable to those of levarterenol.

Antiarrhythmic Drugs.—The appearance of disturbances of cardiac rhythm is common in acute myocardial infarction. If arrhythmias and shock appear together secondarily to myocardial infarction, it is reasonable to assume that the arrhythmia is contributing to the circulatory disturbance and that the elimination of the arrhythmia may be beneficial to the patient. As mentioned, the most serious types of arrhythmia are those associated with a very rapid or a very slow ventricular rate, such as rapid atrial and ventricular tachycardias, uncontrolled atrial flutter and fibrillation, complete heart block, and slow pulse rates due to bigeminal rhythm with ineffective premature beats.

The drug of choice for the control of atrial flutter and fibrillation is digitalis, because the immediate objective is to slow the ventricular rate before a further attempt is made to convert the arrhythmia to sinus mechanism. Shock associated with rapid atrial flutter and fibrillation is one of the few incontestable indications for the intravenous use of digitalis, preferably a rapid-acting digitalis preparation such as ouabain or the glycosides of Digitalis lanata. Digitalis may be used in atrial and nodal tachycardias but is ordinarily contraindicated in ventricular tachycardia.

Quinidine may be effective in controlling all forms of ectopic paroxysmal tachycardias and ectopic beats. Its use in restoring sinus rhythm in atrial flutter and fibrillation should follow digitalization which is effective enough to control the ventricular rate. Quinidine, however, exerts a depressant action upon the myocardium and requires caution when used in myocardial infarction. The parenteral use of quinidine in such cases should be considered a calculated risk in situations in which safer measures are ineffective or the urgency is extreme.

Procainamide (Pronestyl) has a specific effect in terminating and preventing ventricular arrhythmias. It has been used extensively in paroxysmal ventricular tachycardia both orally and intravenously, but whether it is more effective and safer than quinidine has not been definitely established. It has a depressant effect upon the heart and systemic blood pressure similar to that of quinidine.

The acceleration of the slow idioventricular pacemaker in complete heart block can be attempted in two ways. Occasionally, higher degrees of heart block may be caused by increased vagal activity, in which case atropine may be effective. More often, heart block is caused by direct depression or destruction of the conducting tissues. In such cases, the use of those sympathomimetic drugs that have a strong inotropic effect is indicated, namely, ephedrine, epinephrine in oil, isoproterenol (Aludrine, Isonorin, Isuprel, Norisodrine), and phenylpropanolamine (Propadrine). The drug most widely used of late is isoproterenol, which is effective parenterally and sublingually.

Parasympathomimetic drugs, including choline esters and cholinesterase inhibitors such as methacholine (Mecholyl) or neostigmine, may be used either alone or in conjunction with carotid sinus pressure to attempt to terminate paroxysmal supraventricular tachycardia. Potassium salts are used occasionally in shock secondary to myocardial infarction, in the presence of an arrhythmia which may have been caused by a toxic dose of digitalis.

Measures Used To Control Cardiac Failure.—The presence of left ventricular failure or of failure of the left and right sides of the heart is an indication for the use of conventional means of therapy of heart failure. Patients who have previously not had digitalis should be given the full therapeutic dose of the drug, preferably of a rapidly acting preparation; however, this procedure requires more caution than in cardiac failure not associated with myocardial infarction because of the hazard of inducing ventricular tachycardia in the latter condition. Salt restriction is an important part of the therapy of cardiac failure and may be, if necessary, supplemented by the use of diuretic agents.

Other Therapeutic Agents.—The administration of oxygen is widely used in myocardial infarction, particularly when complicated by shock. The physiological rationale for such therapy is questionable because, even in severe shock, the arterial blood is fully saturated, and cyanosis, when present, is caused by peripheral stasis and higher utilization of oxygen in tissues because of the low cardiac output. Oxygen inhalation can supersaturate the arterial blood by its physical solution in plasma. Whether this small additional amount plays a role in overcoming the possible tissue anoxia in the myocardium and other organs is not known. However, in the absence of pulmonary disease, oxygen administration is entirely safe, and its use can be justified empirically.

Pain-relieving agents are of considerable importance because they may be extremely effective in those cases in which vasomotor collapse is caused by ischemic myocardial pain. However, almost all pain-relieving drugs also have a hypotensive effect and in sensitive individuals may lead to nausea, which in itself is a shock-producing agent. Such drugs should be used, therefore, with caution, and the supervision of the patient during their action is essential.

Blood volume expanders formerly enjoyed a brief period of popularity,[10] but later they were largely replaced by pressor amines. Such methods included intravenous infusion of plasma or blood and the intra-arterial administration of blood. The results of these therapeutic maneuvers were equivocal regarding the over-all mortality of shock secondary to myocardial infarction, although temporary favorable effects upon blood pressure levels have been frequently observed.

Comment

The rational approach to the therapy of shock accompanying myocardial infarction is hampered by the inadequate knowledge of the underlying pathophysiology of this type of shock. The prevailing controversy regarding the mechanism of shock centers around the initial factor responsible for the state of shock.

This controversy regarding the factors responsible for shock poses a practical problem of therapy, as to whether peripherally acting or cardiotonic drugs should be employed. The variability of the clinical picture makes interpretation of the results exceedingly difficult. In spite of the widespread interest in the use of pressor amines, which undoubtedly are holding first place in the treatment of this syndrome, enthusiasm of some observers has to be balanced by denial of others that the drugs have any beneficial effect on this condition. The area of uncertainty involves two points: (1) whether the difference demonstrated in animal experiments between pure pressor amines (phenylephrine and methoxamine) and pressor amines with associated cardiotonic action (levarterenol, mephentermine, and metaraminol) can also be demonstrated reliably in the therapeutic range of use in patients, so as to justify the separate pharmacological classification of these drugs; and (2) whether the direct myocardial effect of some of these drugs, if significant, is an asset or a liability in their use in myocardial infarction. Neither of these questions can be answered authoritatively at the present time. The difference between levarterenol and phenylephrine has been studied in a few cases, which, as pointed out, does not constitute a valid argument. It should be noted that there is a similarity between the action of levarterenol, a combined pressor and cardiotonic drug, and the effect of blood volume expanders. However, levarterenol has replaced the latter, largely because of the ease of administration. Blood transfusions, which can relieve shock but have no cardiotonic effect, appear to be less effective in the shock accompanying myocardial infarction than is levarterenol; yet the difference bewteen the two

forms of therapy is not striking and could be accounted for by a more effective regulation of dose. The question of desirability of a cardiotonic action of a pressor amine hinges on the basic mechanism of shock accompanying myocardial infarction, as already discussed. It is generally agreed that a drug with a significant cardiotonic effect has, as a by-product, a tendency to increase myocardial irritability, which is particularly undesirable in myocardial infarction wherein the threshold for dangerous arrhythmias is low. It is believed that the answers to these questions might become available from a carefully organized comparative study, which would investigate the effect of four agents on clinically similar cases of shock secondary to myocardial infarction, namely, (1) pure cardiotonic drugs (digitalis); (2) combined cardiotonic pressor drugs (levarterenol, mephentermine, metaraminol); (3) pure pressor drugs (phenylephrine, methoxamine); and (4) blood volume expanders.

Summary

Shock accompanying acute myocardial infarction is subject to controversy concerning its cause and mechanism. It is suggested that this complication of myocardial infarction cannot be explained on the basis of a single mechanism but rather should be considered a clinical syndrome caused by peripheral vasomotor factors in some instances, by cardiac failure due to intolerable overload of the infarcted ventricle in others, and by inefficient cardiac function caused by arrhythmias in still other cases. At present, because of the unsatisfactory state of understanding of this syndrome, it appears preferable to treat the factor which clinically dominates the picture rather than to formulate a single therapeutic regimen applicable to all cases of shock secondary to myocardial infarction.

Therapeutic measures effective against surgical and other forms of peripheral shock have been applied to treatment of shock secondary to myocardial infarction. These include the use of blood or plasma transfusions given intravenously, intra-arterial blood infusions, and the administration of various pressor amines. All such measures have restored effective blood pressure in many cases, although it is not definitely demonstrated that the high mortality rate from this form of shock has been effectively reduced.

Pressor amines, which at present are considered the treatment of choice for shock, fall into two groups according to their actions in animal experiments, those with purely peripheral vasoconstrictor action and those with combined peripheral and cardiotonic action. It is not yet known whether, in human shock, the difference between the two groups is of practical importance or whether one or the other groups of drugs is superior in the treatment of shock secondary to myocardial infarction.

Shock accompanying myocardial infarction remains an exceedingly serious complication with a very high mortality rate. In spite of considerable enthusiasm concerning the effectiveness of new drugs, there are those who deny that specific antishock measures have any beneficial effects whatsoever.

This study was supported by a grant from the American Heart Association.

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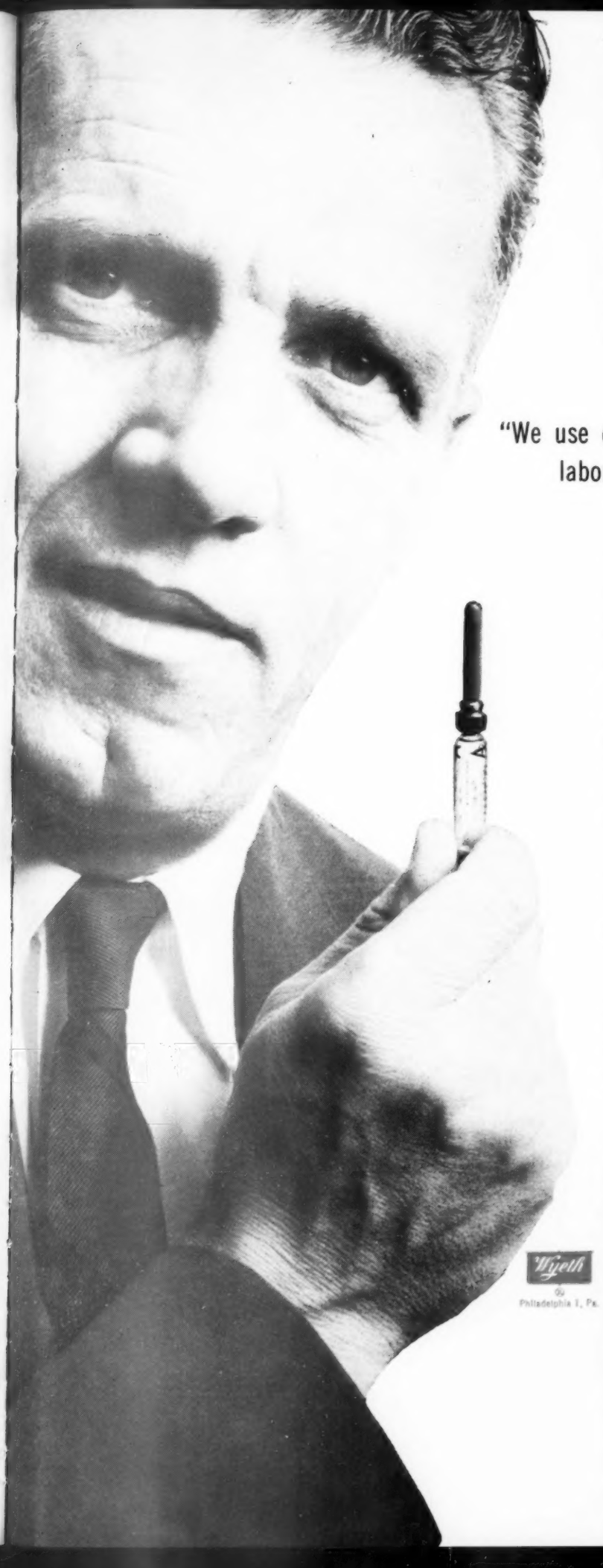

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CHIEF PHARMACIST—Male, married, B.S. working on M.S. Hospital pharmacy experience. Registered Pa. PW-42

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STAFF PHARMACIST—Male, single. Served hospital pharmacy internship, plus 2 years U.S. Army pharmacist. Registered Washington, D.C. PW-110

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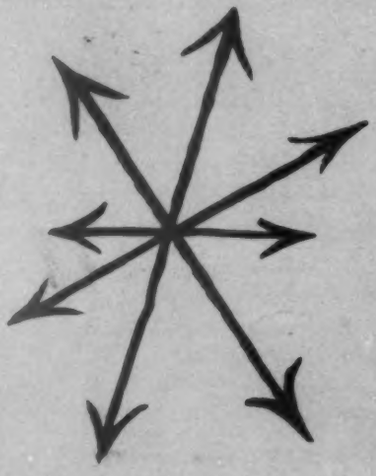

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